CU12-403440 - 34 - P0242

FOUNDED IN 1906 AS THE AMERICAN QUARTERLY OF ROENTGENOLOGY

THE AMERICAN JOURNAL OF ROENTGENOLOGY RADIUM THERAPY AND NUCLEAR MEDICINE

OFFICIAL ORGAN OF

THE AMERICAN ROENTGEN RAY SOCIETY
THE AMERICAN RADIUM SOCIETY

TRAIAN LEUCUTIA, Editor
KENNETH L. KRABBENHOFT, Assistant to the Editor

ASSOCIATE EDITORS
HARRY HAUSER RUSSELL H. MORGAN EDWARD B. D. NEUHAUSER

CONSULTING EDITORIAL BOARD

OSCAR V. BATSON
JOHN CAFFEY
ROSS GOLDEN
PAUL C. HODGES
HOWARD B. HUNT
JOHN H. LAWRENCE
REED M. NESBIT
EUGENE P. PENDERGRASS
LAURISTON S. TAYLOR
OWEN H. WANGENSTEEN
SHIELDS WARREN

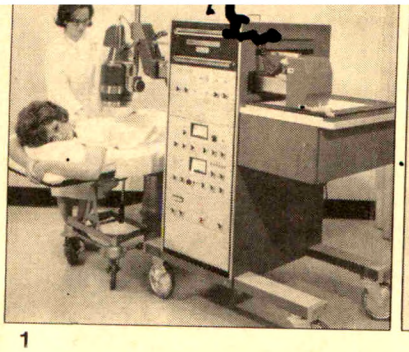
Issued Monthly for the American Roentgen Ray Society by

CHARLES C THOMAS · PUBLISHER · SPRINGFIELD · ILLINOIS · 62703

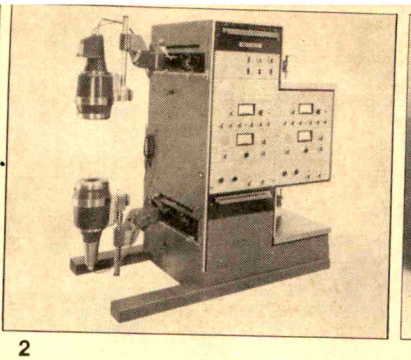
VOLUME 105 JANUARY, 1969 NUMBER 1

Fifty-first Annual Meeting, American Radium Society
Bellevue Stratford Hotel, Philadelphia, Pennsylvania 19102
April 27-30, 1969

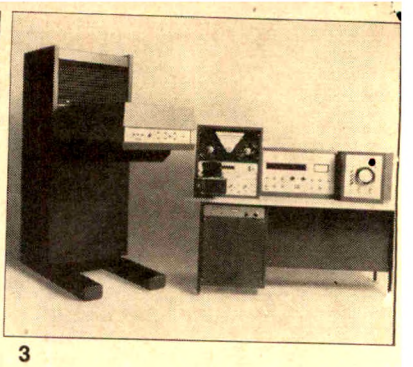
PRELIMINARY PROGRAM



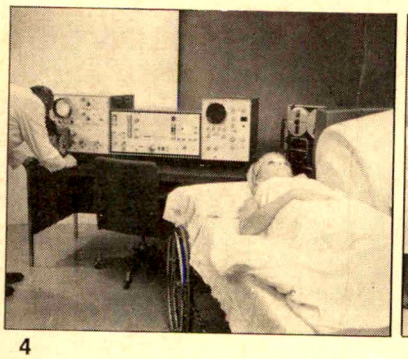
1



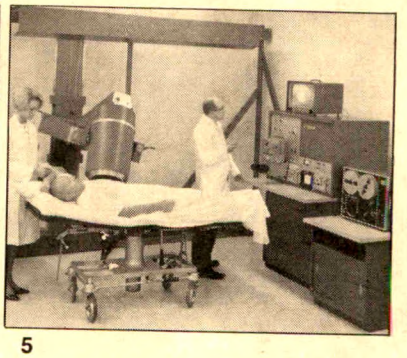
2



3



4



5

1 Magnascanner® 500
2 Dual Magnascanner®
3 Dynapix®
4 Dynacamera™
5 Magnacamera®

"Which is the better choice for gamma imaging, a scanner or a camera?"

(Yes.)

That's much like: "which is better: a plane or a car?" Surely it depends upon the problem at hand.

As it does with gamma imaging. Your one best bet might well be a scanner. Or a camera. You may need both. Sadly, there can be no universal instrument, no all-things-to-all-men system. Consequently, Picker now offers five separate and distinct imaging devices: three are scanners, two are cameras. And this is the most complete line in the world. By far.

The implication is simple: the chances are excellent that Picker has the specific system that precisely matches your needs. Here now are some recognizable user requirements coupled with the appropriate Picker instruments.

Need: small hospital, starting static-imaging, small patient load, modest budget. Or: large hospital needing additional diagnostic confirmation. Solution: Magnascanner® 500. Four out of five nuclear medicine departments start with a Magnascanner. Now over 2000 in use throughout the world. Despite many new features and very high resolution, cost is modest.

Need: specialized static studies involving two views at same time. Solution: Dual Magnascanner®. Provides two large, high resolution scans simultaneously.

Need: heavy static-imaging patient load. Some demand for dynamic function work also. Solution: Dynapix®. High speed static imaging with very high resolution. Also useful for medium speed dynamic function studies.

Need: broad capability for handling both static imaging and dynamic function (and a great deal of it). Solution: Dynacamera™. Very fast instrument providing high resolution. Does both static and dynamic work.

Need: sophisticated dynamic function work at very high speeds. Solution: Magnacamera®. Exceptionally high speed for studying the most rapid dynamic processes.

The conclusion: Picker has a wide selection of imaging systems because there are many imaging needs. The *widest* selection in the world. Suggestion: describe your situation to your local Picker representative and ask him to develop solutions. Or, if more convenient, start by requesting our detailed gamma-imaging brochure. Write Picker Nuclear, 1275. Mamaroneck Avenue, White Plains, N.Y. 10605. Dept. P

PICKER

[FOUNDED IN 1906 AS THE AMERICAN QUARTERLY OF ROENTGENOLOGY]

The AMERICAN JOURNAL OF ROENTGENOLOGY

RADIUM THERAPY AND NUCLEAR MEDICINE

P 24,421

VOLUME 105

JANUARY–APRIL, 1969

CHARLES C THOMAS : SPRINGFIELD, ILLINOIS
1969

COPYRIGHT, 1969
BY AMERICAN ROENTGEN RAY SOCIETY, INC.

CONTENTS OF VOLUME 105

JANUARY, 1969, NUMBER 1

The Role of the Specialist in Medicine and Society; The President's Address, 1968. *John L. Pool, M.D.* ... 3

Esthesioneuroblastomas; A Report of 7 Cases. *Leonidas Castro, M.D., Samuel de la Pava, M.D., and John H. Webster, M.D.* ... 7

Interstitial Radiation in the Management of Malignant Disease of the Facial Structures. *Carl W. Boyer, Jr., Lt. Colonel, MC, USA, Theodore J. Brickner, Jr., Lt. Colonel, MC, USA, Ronald H. Perry, Lt. Colonel, MC, USA, and John G. Maier, Colonel, MC, USA* ... 14

Combined Intra-Arterial Infusion and Radiotherapy for the Treatment of Advanced Cancer of the Head and Neck. *Richard H. Jesse, M.D., Helmuth Goepfert, M.D., Robert D. Lindberg, M.D., and Robert H. Johnson, M.D.* ... 20

Cancer of the Base of the Tongue; 116 Patients Treated Radiotherapeutically in the 11 Year Period 1952 Through 1962. *Paul W. Scanlon, M.D., Edward H. Soule, M.D., Kenneth D. Devine, M.D., and James B. McBean, M.D.* ... 26

Twenty Years' Experience with Radiation Therapy of Medulloblastoma. *Bernard S. Aron, M.D.* ... 37

The Treatment and Prognosis of Medulloblastoma in Children; A Study of 82 Verified Cases. *H. J. G. Bloom, M.D., E. N. K. Wallace, M.B., and J. M. Henk, M.B.* ... 43

Roentgenologic Considerations of the Hyoid Apparatus. *Saar Porrath, M.D.* ... 62

The Management of Cervical Lymph Node Metastasis by Megavoltage Radiotherapy. *G. E. Hanks, M.D., M. A. Bagshaw, M.D., and H. S. Kaplan, M.D.* ... 74

Pre and Postirradiation Azygography: Its Value in Determining Surgical Resectability in Pulmonary Carcinoma. *Carl T. Rinker, M.D., and Arch W. Templeton, M.D.* ... 83

Definitive Radiotherapy of Primary Mediastinal Seminoma. *Malcolm A. Bagshaw, M.D., William T. McLaughlin, M.D., and John D. Earle, M.D.* ... 86

Angiographic Manifestations of Wilms' Tumor; An Observation of Six Cases. *Chien-Hsing Meng, M.D., and Milton Elkin, M.D.* ... 95

Surgical Management of Solid Tumors in Childhood. *Lester W. Martin, M.D.* ... 105

Radium Dosage Patterns in the Treatment of Uterine Carcinoma. *Jacob Spira, Ph.D., and Isamettin Aral, M.D.* ... 110

A Simple Modification of the Stockholm Applicator for the Treatment of Early Cancer of the Uterine Cervix. *Gholam H. Zarghami, M.B., and Samuel S. Kurohara, M.D., with the technical assistance of Lavern Clay* ... 115

A New Rectal Dosimetry Catheter for Use in Radiation Therapy of Carcinoma of the Uterine Cervix. *J. J. Sheldon, M.D., M. Vuksanovic, M.D., G. J. Wold, M.S., and E. A. Fonts, M.D.* ... 120

Enhancement of X-ray Effects on the Small Intestinal Epithelium of Dogs by Actinomycin D. *Joseph P. Concannon, M.D., Roy E. Summers, M.S., John King, D.V.M., George Tcherkow, B.S., Christine Cole, Ph.B., and Edward Rogow, M.D.* ... 126

Response to Radiation Therapy of Osseous Lesions Detected on Radioisotope Bone Scans. *Sheldon Baum, M.D., James H. Davenport, M.D., and Lawrence Silver, M.D.* ... 137

Parosteal Osteosarcoma. *Donald A. Wolfel, M.D., and Peter R. Carter, B.A.* ... 142

Development of Ultrastructural Radiation Injury. *W. R. Hendee, Ph.D., M. A. Alders, B.S., and C. E. Garciga, M.D.* ... 147

Telecobalt Split Field Dosimetry; with Special Reference to Central Penumbral Isodose Separation. *Richard F. Mould, M.Sc.* ... 152

Permanent Interstitial Therapy Using Low Energy and Long Half-Life Radiation Sources. *Joseph E. Scallon, M.D., Charles A. Sondhaus, Ph.D., Samuel L. Snyder, M.D., Bernard H. Feder, M.D., and Walter G. Gunn, M.D.* ... 157

Clinical Application of Computer Dosimetry in Interstitial Radium Therapy. *Joseph R. Castro, M.D., Robert D. Lindberg, M.D., and Gilbert H. Fletcher, M.D.* ... 165

Current Techniques with 6–18 mev. Electron Beam. *Norah DuV. Tapley, M.D., and Gilbert H. Fletcher, M.D.* ... 172

The Dosimetric and Biologic Problems Posed by Electron Beam Therapy. *M. Tubiana* ... 178

Modulation Transfer Functions of the Ionization Chamber. *Suguru Uchida, E.D.* ... 185

The Effects of Partial Irradiation on Tail Regeneration in Adult Siredon Mexicanum. *V. V. Brunst, Sc.D.* ... 196

Officers ... 207

Editorials
The Fifty-first Annual Meeting of the American Radium Society. *J. A. del Regato, M.D.* ... 208
Arthur C. Singleton, M.D., 1900–1968. *M. R. Hall, M.D.* ... 210
The American Radium Society, Fifty-first Annual Meeting: Preliminary Program ... 212
International Commission on Radiation Units and Measurements (ICRU) ... 215
News Items ... 216
Book Review ... 220
Books Received ... 220
Society Proceedings ... 222
Abstracts of Radiological Literature ... 228

February, 1969, Number 2

The Lung: The Challenge of Nuclear Medicine. *James Leland Quinn, III* ... 251
Precise Alignment of X-ray Beams for Stereotactic Surgery. *Paul C. Hodges, M.D., and Francisco Garcia-Bengochea, M.D.* ... 260
An Image Enlargement Scale for Stereotactic Surgery. *Edwin M. Todd, M.D., and Benjamin L. Crue, Jr., M.D.* ... 270
Stereotaxic Transsphenoidal Biopsy and Cryosurgery of Pituitary Tumors. *Robert W. Rand, Ph.D., M.D., Gunnar Heuser, Ph.D., M.D., Alfred Dashe, M.D., Donald Adams, M.D., and Nathan Roth, M.D.* ... 273
Localization of the Calcified Pineal Body on Lateral Roentgenograms. *Captain Ronald P. Pawl, MC, USA, and Captain Arthur K. Walter, MC, USA* ... 287
Suprasellar Subarachnoid Cysts. *André Sansregret, M.D., Roger Ledoux, M.D., Fernand Duplantis, M.D., Christian Lamoureux, M.D., Alcide Chapdelaine, M.D., and Pierre Leblanc, M.D.* ... 291
Congenital Arachnoid Cysts. *Yahya M. Berkmen, M.D., Jack Brucher, M.D., and James H. Salmon, M.D.* ... 298
Post-Traumatic Leptomeningeal Cysts. *Frank H. Gruber, M.D.* ... 305
Cartilaginous Tumors of the Base of Skull. *Hideyo Minagi, M.D., and Thomas H. Newton, M.D.* ... 308
The Calvarial "Doughnut Lesion": A Previously Undescribed Entity. *Theodore E. Keats, M.D., and John F. Holt, M.D.* ... 314
Calvarial Bone Defects in Neurofibromatosis: A Case Report. *M. M. Saha, K. N. Agarwal, and O. P. Bhardwaj* ... 319
Sarcoidosis of the Skull; Report of a Case. *Oscar A. Turner, M.D., and Sanford R. Weiss, M.D.* ... 322
An Unusual Angiographic Appearance of Cerebral Arteriovenous Malformations. *LTC William M. Hammon, MC, USA* ... 326
Aneurysms of the Superficial Temporal Artery. *Charles B. Wilson, M.D.* ... 331
Posterior Fossa Aneurysms Presenting As Mass Lesions. *H. F. W. Pribram, M.D., D.M.R.D., J. D. Hudson, M.D., and Robert J. Joynt, M.D.* ... 334
Vascular Malformations of the Posterior Fossa Including the Tentorial Hiatus. *Lawrence H. Zingesser, M.D., Mannie M. Schechter, M.D., E. Leon Kier, M.D., and Mark S. O'Brien, M.D.* ... 341
Selective Third Ventricular Catheterization for Pantopaque Ventriculography. *Harold A. Wilkinson, M.D.* ... 348
Idiopathic Familial Cerebrovascular Ferrocalcinosis (Fahr's Disease) and Review of Differential Diagnosis of Intracranial Calcification in Children. *Donald P. Babbitt, M.D., T. Tang, M.D., J. Dobbs, M.D., and R. Berk, M.D.* ... 352
Autotomography Applied to the Pharynx and Dens; A Simple Wand for the Technique. *Edwin L. Lame, M.D., and Thomas J. Redick* ... 359
Roentgenographic Examination of Foramen Transversarium of Axis; Practical Considerations. *Trygve O. Gabrielsen* ... 361
Calcification of the Posterior Longitudinal Ligament: A Cause of Cervical Myelopathy. *Hideyo Minagi, M.D., and Arthur T. Gronner, M.D.* ... 365
Roentgenographic Correlations in Cervical Spondylosis. *H. A. Wilkinson, M.D., M. L. LeMay, M.D., and E. J. Ferris, M.D.* ... 370
The Neurologic Complications of Paget's Disease in the Cervical Spine. *Frieda Feldman, M.D., and William B. Seaman, M.D.* ... 375
Spontaneous Epidural Spinal Hemorrhage. *Martin E. Harris, M.D.* ... 383
Intraspinal Dermoids and Epidermoids. *S. K. Gupta, M.D., D.M.R., and Y. P. Bhandari, M.D., D.M.R.E.* ... 386
The Occult Intrasacral Meningocele. *Irving S. Young, M.D., and André J. Bruwer, M.D.* ... 390
Schistosomiasis of the Spinal Cord. *Arnold Chait, M.D., and William E. Gannon, M.D.* ... 400

Effect of Parabens on the Permeability of the Blood: Brain Barrier to Water-Soluble Radiopaque Media. *William H. Strain, Ph.D., Robert J. Rivers, Jr., M.D., Richard J. O'Reilly, M.D., Daniel T. Danahy, M.D., Martin R. Thomas, M.D., and Robert M. Wilson* 404
A Simple Biplane Myelographic Table. *H. F. W. Pribram, M.D., D.M.R.D., R. E. Kitchen, B.S.E.E., and M. P. Neal, Jr., M.D.* 411
Ultrasonic Diagnosis of Subdural Hematomas. *Jeffrey Rothman, M.D., Stanley Shatsky, B.S., Irvin Kricheff, M.D., and Norman Chase, M.D.* 413
B-Scan Ultrasound Exploration of Neoplastic Disease. *Bruno Damascelli, M.D., Franca Fossati, M.D., Tito Livraghi, M.D., and Aldo Severini, M.D.* 428
Echographic Diagnosis of Retroperitoneal Lymph Node Enlargement; Ultrasound Scanning Technique and Diagnostic Findings. *W. Michael Asher, M.D., and Atis K. Freimanis, M.D.* 438
A Modified Technique of Ultrasonography for the Detection and Differential Diagnosis of Breast Lesions. *Frank H. DeLand* 446
Officers 453
Editorials
Who Should Do Echography? *Atis K. Freimanis, M.D.* 454
W. Walter Wasson, M.D., 1884–1968. *Wendell G. Scott, M.D.* 456
News Items 459
Book Reviews 462
Books Received 463
Society Proceedings 465
Abstracts of Radiological Literature 471

March, 1969, Number 3

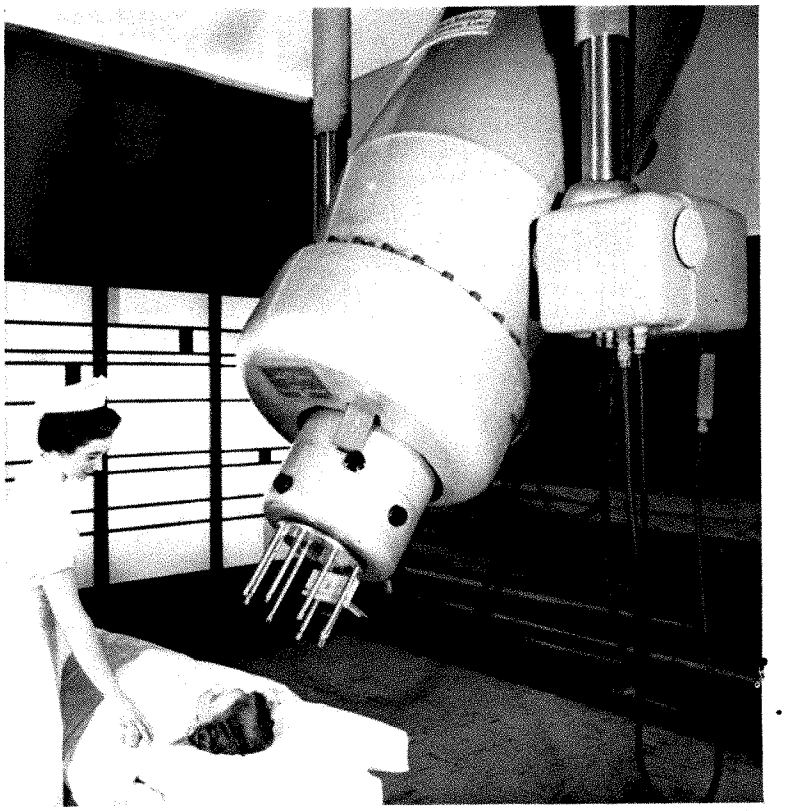
The Centralization of Cancer Services—How Far Should It Go?; The Janeway Lecture, 1968. *W. G. Cosbie, M.B.* 487
The Value of Radiotherapy in the Management of Esophageal Cancer. *J. G. Pearson* 500
Some Opinions on Treatment of Cancer of the Esophagus. *W. D. Rider, M.B., and R. Diaz Mendoza, M.D.* 514
Dosimetric Considerations in Cobalt 60 Rotational Therapy for Esophageal Lesions; A Comparison of Transit and Intraluminal Dose Measurement. *David B. Goldenberg, M.D., U. V. Gopala Rao, ScD., Stewart Lott, M.D., and Joseph Digel, R.T.* 518
Surgical and Radiation Treatment of Cancer of the Thoracic Esophagus. *John T. Goodner, M.D.* 523
Radiation Induced Neoplasia Following External Beam Therapy for Children with Retinoblastoma. *Robert H. Sagerman, M.D., J. Robert Cassady, M.D., Patricia Tretter, M.D., and Robert M. Ellsworth, M.D.* 529
The Influence of the Relationship "Local Tumor Extent-Time" Upon the Evolution of Tumors of the Nasopharynx. *J. F. Bohorquez, M.D.* 536
Radiation Therapy of Carcinoma of the Anterior Nasal Cavity. *Wayne P. Whitcomb, M.D.* 550
Hydroxyurea: A Radiosensitizer in the Treatment of Neoplasms of the Head and Neck. *George J. Richards, Jr., M.D., and Robert G. Chambers, M.D.* 555
Long Time Survivals of Patients with Cancer of the Eye and Surrounding Structures Treated with Radiation Therapy. *Charles L. Martin, E.E., M.D.* 566
An Evaluation of the Manchester System of Treatment of Carcinoma of the Cervix. *George Schwarz, M.D.* 579
The Combination of External Irradiation and Curietherapy Used Preoperatively in Adenocarcinoma of the Endometrium. *Victor A. Marcial, José M. Tomé, and Jeannie Ubiñas* 586
Recurrent Cancer of the Corpus Uteri; Techniques and Results of Treatment. *Ahmed O. Badib, M.D., Samuel S. Kurohara, M.D., Antonio A. Beitia, M.D., and John H. Webster, M.D.* 596
Adenocarcinoma of the Uterus. *Luis Delclos, M.D., Gilbert H. Fletcher, M.D., Augusto G. Gutierrez, M.D., and Felix N. Rutledge, M.D.* 603
Afterloading Vaginal Ovoids. *Allan E. Green, Jr., M.D., John R. Broadwater, M.D., and James A. Hancock, Jr., Major, USAF, B.S.C.* 609
The Role of Preoperative Irradiation in the Treatment of Carcinoma of the Ovary. *Jerome M. Vaeth and Franz J. Buschke* 614
The Clinical Course of Hodgkin's Disease and Other Malignant Lymphomas Treated with Radical Radiation Therapy. *Leonard R. Prosnitz, M.D., Samuel Hellman, M.D., Carl F. Von Essen, M.D., and Morton M. Kligerman, M.D.* 618
Curative Treatment of Hodgkin's Disease. *John F. Hynes, M.D.* 629

Cutaneous Reactions after Radiation Therapy; Report of 7 Cases. *William S. Maxfield, M.D., and William P. Coleman, M.D.* ... 636
Dystrophic Epidermolysis Bullosa; Tolerance of the Bed and Response of Multifocal Squamous Cell Carcinomas to Ionizing Radiation: Report of a Case. *Robert W. Edland, M.D.* ... 644
A Light Analog System for Radiotherapy Planning. *Gerald S. Freedman, B.M.E., and Paul N. Goodwin, Ph.D.* ... 648
Radiation Tolerance of the Thoracic Spinal Cord. *Theodore L. Phillips, M.D., and Franz Buschke, M.D.* ... 659
Changing Perspectives in Oxygen Breathing and Radiation Therapy. *Philip Rubin, M.D., Colin A. Poulter, M.B., and Raymond S. Quick, B.Sc.* ... 665
Isotope Renography and Renal Arteriography in the Evaluation of Renal Transplants. *Harold D. Davidson, M.D., Merle K. Loken, Ph.D., and Kurt Amplatz, M.D.* ... 682
The Plugging of Leaks in Radium Containers. *M. L. Rozenfeld, M.S., and E. W. Mason, B.S.* ... 689
Officers ... 698
Editorial
The Reynolds Historical Library. *Traian Leucutia, M.D.* ... 699
News Items ... 702
Book Review ... 703
Books Received ... 703
Society Proceedings ... 705
Abstracts of Radiological Literature ... 711

April, 1969, Number 4

Fluorescent Thyroid Scanning. *Paul B. Hoffer, M.D.* ... 721
Serial Brain Scanning with Technetium 99m Pertechnetate in Cerebral Infarction. *Michael S. Usher, M.D., and James L. Quinn, III, M.D.* ... 728
Radiation Response in Relation to the Cell Cycle In Vivo. *Jacob I. Fabrikant* ... 734
Patterns of Protein Synthesis in the HeLa Cancer Cell. *Gerald M. Kolodny, M.D.* ... 746
Roentgenologic Studies of Cerebrospinal Fluid Formation in the Dog. *D. Gordon Potts, M.D., and Richard M. Bergland, M.D.* ... 756
Lipid Embolism to the Brain Following Lymphography; Case Report and Experimental Study. *J. W. Davidson, M.B.* ... 763
Contrast-Vasoconstrictor Mixtures in Angiography. *Paul C. Kahn, M.D., with the technical assistance of Joseph P. Zeppieri, A.B., and Gerald S. Lorch, B.S.* ... 772
Effect of Angiocardiography on Fluid and Electrolyte Balance. *Aaron R. Levin, M.R.C.P. (Edin.), Herman Grossman, M.D., Edward T. Schubert, Ph.D., Patricia Winchester, M.D., and Angela Gilladoga, M.D.* ... 777
Coronary Arteriography in Hypercholesterolemic Patients. *Harold A. Baltaxe, M.D., Kurt Amplatz, M.D., Richard L. Varco, M.D., and Henry Buchwald, M.D.* ... 784
Effects of Ionizing Radiation upon the Immature Rabbit Larynx. *Frederick J. Bonte, M.D., Vernie L. Stembridge, M.D., and James D. Reef, M.D.* ... 791
Vascular Structure of Glioblastomas. *J. H. Scatliff, M.D., W. B. Radcliffe, M.D., H. H. Pittman, B.S., and C. H. Park, M.D.* ... 795
The Basis for Segmental Sequential Irradiation in Hodgkin's Disease: Extended vs. Local Fields in the Radiocurability of the SJL/J Mouse Hodgkin's-Like Reticulum Cell Sarcoma. *Philip Rubin and Glenn Haluska, with the technical assistance of George Miller* ... 806
The Basis for Segmental Sequential Irradiation in Hodgkin's Disease: Clinical Experience of Patterns of Recurrence. *P. Rubin, G. Haluska and C. A. Poulter* ... 814
The Lamina Dura (L. D.) of the Maxillary Antrum: Its Value in Roentgen Diagnosis. *T. El Gammal, M.B., and Theodore E. Keats, M.D.* ... 830
Tomography of the Temporal Bone in Paget's Disease. *Jerry P. Petasnick, M.D.* ... 838
The Supracondylar Process and Its Fracture. *Alex Newman, M.D.* ... 844
Triangular Cartilage Calcification in the Wrists: Its Incidence in Elderly Persons. *Wylie J. Dodds, M.D., and Howard L. Steinbach, M.D.* ... 850
A Study of Inter- and Intra-Observer Error in Reading Plain Roentgenograms of the Hands; "To Err is Human." *John H. Bland, M.D., A. Bradley Soule, M.D., Frederick W. VanBuskirk, M.D., Estelle Brown, B.S., and Ruth V. Clayton* ... 853
Epiphyseal Dysostosis. *Howard L. Steinbach, M.D., and Robert A. Brown, M.D.* ... 860

Use of a Digital Computer in the Measurement of Roentgenographic Bone Density. *Fred B. Vogt, M.D., Louis S. Meharg, Ph.D., and Pauline Beery Mack, Ph.D.* 870
Congenital Arteriovenous Malformation of the Foot. *L. E. Kellerhouse, M.D., and K. Ranniger, M.D.* 877
Mammographic Technique: Need for Routine Spot Roentgenograms. *M. B. Hermel, M.D., J. Gershon-Cohen, M.D., and R. N. Byrne, M.D.* 880
The Use of Hysterography in the Detection of Hydatidiform Mole. *Edward I. Greenbaum, M.D., G. Podolak, M.D., and B. J. O'Loughlin, Ph.D.* 885
A Roentgenologic Rule and Pelvimetry Technique. *T. H. Johnson, Jr., M.D., and T. A. Reagan, R. T.* 890
Recovery of Detached Intravascular Catheter or Guide Wire Fragments; A Proposed Method. *Joseph L. Curry, M.D.* 894
Skin Exposure from Handling Syringes Containing Radioactive Isotopes. *R. S. Clayton, M.D., J. E. White, M.D., M. Brieden and A. Rodriguez, R.T.* 897
The Independent Radiation Monitor (I.R.M.). *Paul M. Kroening, M.D., and Raymond Mucha* 900
Three Dimensional Roentgenography. *J. B. Garrison, D. G. Grant, W. H. Guier, and R. J. Johns* 903
The Line Spread-Function and the Modulation Transfer Function of X-Ray Fluorescent Screen-Film Systems—Problems with Double-Coated Films. *G. Lubberts, M.S.* 909
Officers 918
Editorials
Winds of Change Pass Over the A.U.R. *Stanley M. Rogoff, M.D.* 919
Palmer E. Wigby, M.D., 1903–1968. *Curtis H. Burge, M.D.* 921
News Items 922
Books Received 924
Society Proceedings 925
Abstracts of Radiological Literature 931
Subject Index to Volume 105 938
Author Index to Volume 105 949

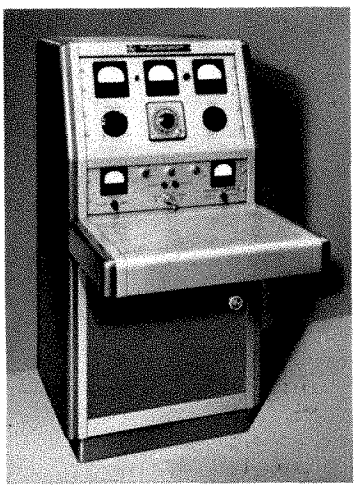


Improved Model AM Van de Graaff is the result of experience gained in 40 previous installations.

IMPROVED *Van de Graaff*® ACCELERATOR MEETS THE MODERN NEED FOR LOW-COST PRECISION THERAPY

Today's Model AM 2 MeV Van de Graaff Therapy Unit continues to keep pace with the trend to low-cost precision therapy in leading hospitals and cancer clinics throughout the Free World. And for five good reasons:

- Its less than 3 mm "point source" of x-rays allows optimum technics for both large and small treatment fields.
- Its treatment beam is accompanied by negligible penumbra.
- Its Roentgen output exceeds that of a 5000 curie cobalt source.
- Its x-ray output will not fall off. You can hold treatment techniques and parameters constant.
- It can be operated easily by a technician without a staff physicist in attendance.



The Model AM Van de Graaff is a reliable, proven source of high-energy radiation. It offers more roentgens-per-dollar and has demonstrated less overall cost-per-treatment than any other comparable supervoltage source available today — including radioisotopes.

Full time use of the reliable Model AM 2 MeV Van de Graaff Therapy Unit will amplify your technic range and expand your patient handling capacity. It is backed by the international reputation of the leading manufacturer of particle accelerators — High Voltage Engineering Corporation. Write Medical Sales.

Today's Model AM is routinely operated by an easily-trained technician.

HIGH VOLTAGE ENGINEERING CORPORATION
BURLINGTON, MASSACHUSETTS

GENERAL INFORMATION

Manuscripts offered for publication and other correspondence relating to the editorial management and books for review should be sent to Dr. Traian Leucutia, Editor, 401 Professional Building, Detroit, Michigan 48201. Contributions may be sent in foreign languages and will be translated if found acceptable. Original articles are published with the understanding that they are contributed exclusively to THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE.

A certain number of illustrations will be supplied free of cost; but special arrangements must be made with the Editor and Publisher for excess illustrations and elaborate tables.

Fifty reprints are furnished without charge to authors. Additional reprints may be purchased according to a scale of prices that accompanies galley proofs. As soon as each issue is printed, the type is destroyed except for reprint orders *in hand*. Reprint orders *must* be returned with corrected galley proof to the Editorial Office if additional reprints are desired.

Correspondence regarding subscriptions, advertisements, and other business relating to THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE should be addressed to Charles C Thomas, Publisher 301–327 East Lawrence Avenue, Springfield, Illinois 62703. (All requests to be submitted in writing.)

Manuscripts should be typewritten, with double spacing, and good margins (not on thin paper) and the *original* should be sent to the Editor. The author should keep a carbon copy, as the original is not returned. The name of the author should appear on each sheet of manuscript. Tabular materials should be typed on separate sheets; likewise bibliographical lists, footnotes, etc.

Drawings and charts for reproduction should be made in black (*never* in blue). Photographic prints of plates or slides on glossy paper produce the best half-tones.

All photographs and drawings intended for illustrations should be numbered, the top plainly indicated, and an abbreviated title of the paper placed on the back of *each one*.

Legends for illustrations should be typewritten in a single list, double spaced, with numbers corresponding to those on the photographs and drawings, instead of attaching each legend to its corresponding figure.

Care in preparation of bibliographies will save much time and correspondence. Each reference in a bibliography should include the following information in the order indicated: Name of the author with initials; title of the article; name of the periodical; year, volume and pages. It is requested that the authors use the following as model:

1. Olcott, C. T., and Dooley, S. W. Agenesis of lung of infant. *Am. J. Dis. Child.*, 1943, *65*, 766–780.

The month should be given if the reference is to an issue of the current year. An alphabetical arrangement of the authors is requested.

The author should always place his full address somewhere on his manuscript. This is very important and is often omitted.

For information regarding membership in the American Roentgen Ray Society, address the Chairman of the Executive Council, Dr. E. F. Van Epps, Duke University, Durham, North Carolina 27706.

For information regarding the program of the annual meeting of the American Roentgen Ray Society, address the President-Elect, Dr. James C. Cook, LL 14 Professional Plaza, 3790 Woodward Avenue, Detroit, Michigan 48201.

For information regarding membership in the American Radium Society, address the Secretary, Dr. John V. Blady, The Parkway House, 2201 Benjamin Franklin Parkway, Philadelphia, Pennsylvania 19130.

For information regarding the program of the annual meeting of the American Radium Society, address the President, Dr. Juan A. del Regato, Penrose Cancer Hospital, 2215 North Cascade Avenue, Colorado Springs, Colorado 80907.

THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE is owned, maintained by, and in the interests of the American Roentgen Ray Society, Inc. It is issued monthly by Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Illinois 62703. THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE does not hold itself responsible for any statements made or opinions expressed by any contributors in any article published in its columns.

Delivery is not guaranteed. Replacements are not guaranteed nor promised, but will be attempted if extra single copies are available and only if requested within 30 days from first of month following publication (17th of month) for domestic subscribers and 60 days for foreign subscribers.

Annual subscription price is as follows: United States, U. S. Possessions, U. S. Trusteeships, Pan-American Union, and Canada, $20.00; other countries $22.00. Prices for back volumes quoted on application. Extra single copies of back issues, if available, $2.00, postpaid. Current subscriptions may begin with any issue. Remittance should be sent to CHARLES C THOMAS, PUBLISHER, 301–327 East Lawrence Avenue, Springfield, Illinois 62703, U.S.A.

ADDRESS CHANGE—When a change of address is necessary please allow at least 60 days notice and preferably 90 days. When ordering a change of address, send the Publisher both the old and new address.

Entered as Second-class at Springfield, Illinois under the Act of March 3, 1879. Printed in U.S.A.
Second-class postage paid at Springfield, Illinois and at additional mailing offices.

Copyright © 1969, by AMERICAN ROENTGEN RAY SOCIETY, Inc. No part may be duplicated or reproduced without permission of both the Publisher and the Editor.

THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE

VOL. 105 JANUARY, 1969 NO. 1

TABLE OF CONTENTS

The Role of the Specialist in Medicine and Society; The President's Address, 1968. JOHN L. POOL, M.D. 3

Esthesioneuroblastomas; A Report of 7 Cases. LEONIDAS CASTRO, M.D., SAMUEL DE LA PAVA, M.D., AND JOHN H. WEBSTER, M.D. . . . 7

Interstitial Radiation in the Management of Malignant Disease of the Facial Structures. CARL W. BOYER, JR., LT. COLONEL, MC, USA, THEODORE J. BRICKNER, JR., LT. COLONEL, MC, USA, RONALD H. PERRY, LT. COLONEL, MC, USA, AND JOHN G. MAIER, COLONEL, MC, USA . . 14

Combined Intra-Arterial Infusion and Radiotherapy for the Treatment of Advanced Cancer of the Head and Neck. RICHARD H. JESSE, M.D., HELMUTH GOEPFERT, M.D., ROBERT D. LINDBERG, M.D., AND ROBERT H. JOHNSON, M.D. 20

Cancer of the Base of the Tongue; 116 Patients Treated Radiotherapeutically in the 11 Year Period 1952 Through 1962. PAUL W. SCANLON, M.D., EDWARD H. SOULE, M.D., KENNETH D. DEVINE, M.D., AND JAMES B. MCBEAN, M.D. 26

Twenty Years' Experience with Radiation Therapy of Medulloblastoma. BERNARD S. ARON, M.D. 37

The Treatment and Prognosis of Medulloblastoma in Children; A Study of 82 Verified Cases. H. J. G. BLOOM, M.D., E. N. K. WALLACE, M.B., AND J. M. HENK, M.B. 43

Roentgenologic Considerations of the Hyoid Apparatus. SAAR PORRATH, M.D. 63

The Management of Cervical Lymph Node Metastasis by Megavoltage Radiotherapy. G. E. HANKS, M.D., M. A. BAGSHAW, M.D., AND H. S. KAPLAN, M.D. 74

Pre and Postirradiation Azygography: Its Value in Determining Surgical Resectability in Pulmonary Carcinoma. CARL T. RINKER, M.D., AND ARCH W. TEMPLETON, M.D. 83

Definitive Radiotherapy of Primary Mediastinal Seminoma. MALCOLM A. BAGSHAW, M.D., WILLIAM T. MCLAUGHLIN, M.D., AND JOHN D. EARLE, M.D. 86

Angiographic Manifestations of Wilms' Tumor; An Observation of Six Cases. CHIEN-HSING MENG, M.D., AND MILTON ELKIN, M.D. . . . 95

Surgical Management of Solid Tumors in Childhood. LESTER W. MARTIN, M.D. 105

(Continued on page iv)

Radium Dosage Patterns in the Treatment of Uterine Carcinoma. JACOB SPIRA, PH.D., AND ISAMETTIN ARAL, M.D. 110
A Simple Modification of the Stockholm Applicator for the Treatment of Early Cancer of the Uterine Cervix. GHOLAM H. ZARGHAMI, M.B., AND SAMUEL S. KUROHARA, M.D., with the technical assistance of LAVERN CLAY 115
A New Rectal Dosimetry Catheter for Use in Radiation Therapy of Carcinoma of the Uterine Cervix. J. J. SHELDON, M.D., M. VUKSANOVIC, M.D., G. J. WOLD, M.S., AND E. A. FONTS, M.D. 120
Enhancement of X-Ray Effects on the Small Intestinal Epithelium of Dogs by Actinomycin D. JOSEPH P. CONCANNON, M.D., ROY E. SUMMERS, M.S. JOHN KING, D.V.M., GEORGE TCHERKOW, B.S., CHRISTINE COLE, PH.B., AND EDWARD ROGOW, M.D. 126
Response to Radiation Therapy of Osseous Lesions Detected on Radioisotope Bone Scans. SHELDON BAUM, M.D., JAMES H. DAVENPORT, M.D., AND LAWRENCE SILVER, M.D. 137
Parosteal Osteosarcoma. DONALD A. WOLFEL, M.D., AND PETER R. CARTER, B.A. 142
Development of Ultrastructural Radiation Injury. W. R. HENDEE, PH.D., M. A. ALDERS, B.S., AND C. E. GARCIGA, M.D. 147
Telecobalt Split Field Dosimetry; with Special Reference to Central Penumbral Isodose Separation. RICHARD F. MOULD, M.Sc. 152
Permanent Interstitial Therapy Using Low Energy and Long Half-Life Radiation Sources. JOSEPH E. SCALLON, M.D., CHARLES A. SONDHAUS, PH.D., SAMUEL L. SNYDER, M.D., BERNARD H. FEDER, M.D., AND WALTER G. GUNN, M.D. 157
Clinical Application of Computer Dosimetry in Interstitial Radium Therapy. JOSEPH R. CASTRO, M.D., ROBERT D. LINDBERG, M.D., AND GILBERT H. FLETCHER, M.D. 165
Current Techniques with 6–18 mev. Electron Beam. NORAH DUV. TAPLEY, M.D., AND GILBERT H. FLETCHER, M.D. 172
The Dosimetric and Biologic Problems Posed by Electron Beam Therapy. M. TUBIANA 178
Modulation Transfer Functions of the Ionization Chamber. SUGURU UCHIDA, E.D. 185
The Effects of Partial Irradiation on Tail Regeneration in Adult Siredon Mexicanum. V. V. BRUNST, SC.D. 196
Officers 207
Editorials
The Fifty-first Annual Meeting of the American Radium Society. J. A. DEL REGATO, M.D.. 208
Arthur C. Singleton, M.D., 1900–1968. M. R. HALL, M.D. 210
The American Radium Society, Fifty-first Annual Meeting: Preliminary Program 212
International Commission on Radiation Units and Measurements (ICRU) . 215
News Items. 216
Book Review 220
Books Received 220
Society Proceedings 222
Abstracts of Radiological Literature 228

"prep" the colon with pleasant-tasting X-PREP Liquid

(standardized extract of senna fruit)

Specifically designed for preradiographic bowel evacuation, X-PREP Liquid permits excellent visualization in G.I. and urologic roentgenography.

No significant gas shadows. No residual oil droplets.

X-PREP Liquid reduces or eliminates the need for enemas prior to radiography.

And delicious X-PREP Liquid gives a welcome reprieve for your patients from the obnoxious taste of castor oil.

Easy-to-take, X-PREP Liquid is also easy to administer. Premixed and premeasured, this effective bowel evacuant comes in small, single-dose bottles—to be taken between 2 and 4 p.m. on the day prior to radiography. Patients should be advised to expect strong purgative action.

Contraindication: Acute surgical abdomen.
Supplied: Ready-to-drink in 2½ oz. bottles (complete adult dose).
Also available: X-PREP Powder (standardized senna concentrate). Mixed with water, ¾ oz. canister provides complete adult dose.

GRAY PHARMACEUTICAL CO., AFFILIATE,
THE PURDUE FREDERICK COMPANY,
Yonkers, New York

© COPYRIGHT 1968, GRAY PHARMACEUTICAL CO. E-25166R

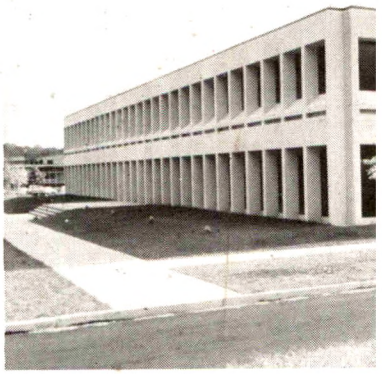


for a clear picture



X-ray visualization following barium enema. Patient prepared with single dose of X-PREP Liquid—2½ oz. Note absence of fecal retention.
Courtesy of Statman, A. J.: An Effective Single-Dose Evacuant, J. M. Soc. New Jersey 63:95 (March) 1966.

This
is the pl
our
custom
built





BETTER TECHNICAL SERVICE:
The Ilford film dark room (above) is one of s
designed to provide top-notch technical inf
tion to Ilford customers.

ILFORD IN

33 million
Administered Doses of

Telepaque®

brand of **iopanoic acid**

A Record of Clinical Experience
and Safety Without Parallel

Winthrop



The real story is on the inside of the Ultima X-Ray Control Unit

The story is modular unit construction. That's what makes the Ultima X-Ray Control Unit unique. It means we can build it to your exact requirements without the cost or waiting normally associated with custom construction. You can actually choose from 1056 different possible combinations of controls, timer modes, and special features. You can also choose from either 400 or 600 MA models with solid state or thermionic valve high-voltage rectified transformers.

After you make your selection, Standard will quickly assemble an Ultima from pre-fabricated, pre-tested modular component units ready in stock. Result? The control unit to fit your exact requirements in the fastest possible time.

You get more than just choice with the Ultima X-Ray Control Unit. You get flexibility too. At any time, simply by changing modules, you can modify or up-grade the Ultima to meet new requirements. For example, if you wish to convert from the control of conventional 60-cycle x-ray tubes to control of high-speed 180-cycle x-ray tubes, the Ultima can be modified quickly, on-the-spot, and with minimum cost.

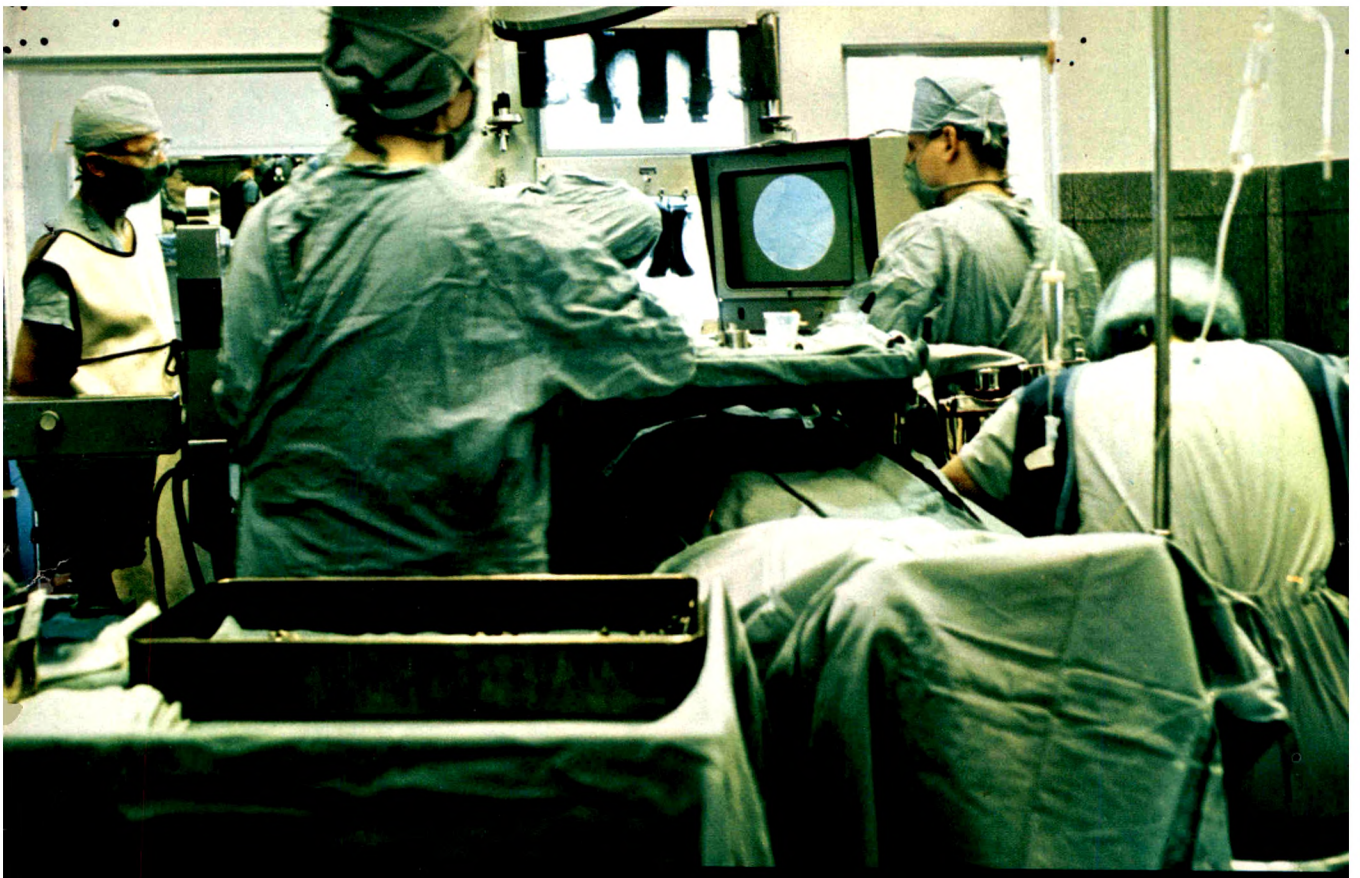
Servicing is simplified too. Modules and components can be serviced or replaced individually as required without dismantling the entire unit. Careful design has kept all parts readily accessible and easy to reach.

Most important, you benefit from Standard's 53 years of experience in producing durable, dependable, and quality x-ray equipment. Every bit of this experience has gone into the design and production of the Ultima X-Ray Control Unit.

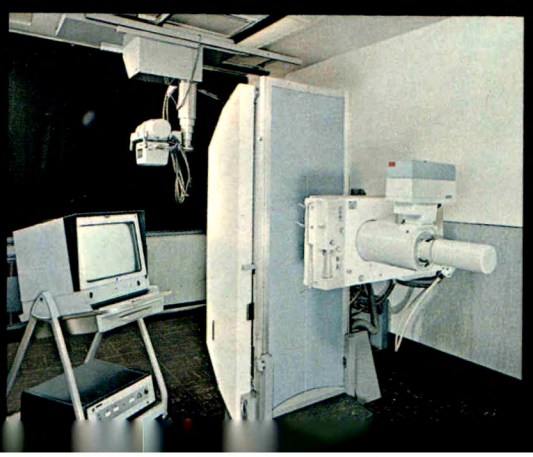
Your Standard X-Ray dealer will be happy to explain the wide choice of options and other features available to you. He can also tell you about Standard's other superior quality x-ray equipment. For the name of your local dealer and a copy of our new catalog, just contact us.

STANDARD

STANDARD X-RAY COMPANY
a subsidiary of Cenco Instruments Corp.
1932 N. Burling St., Chicago, Ill. 60614

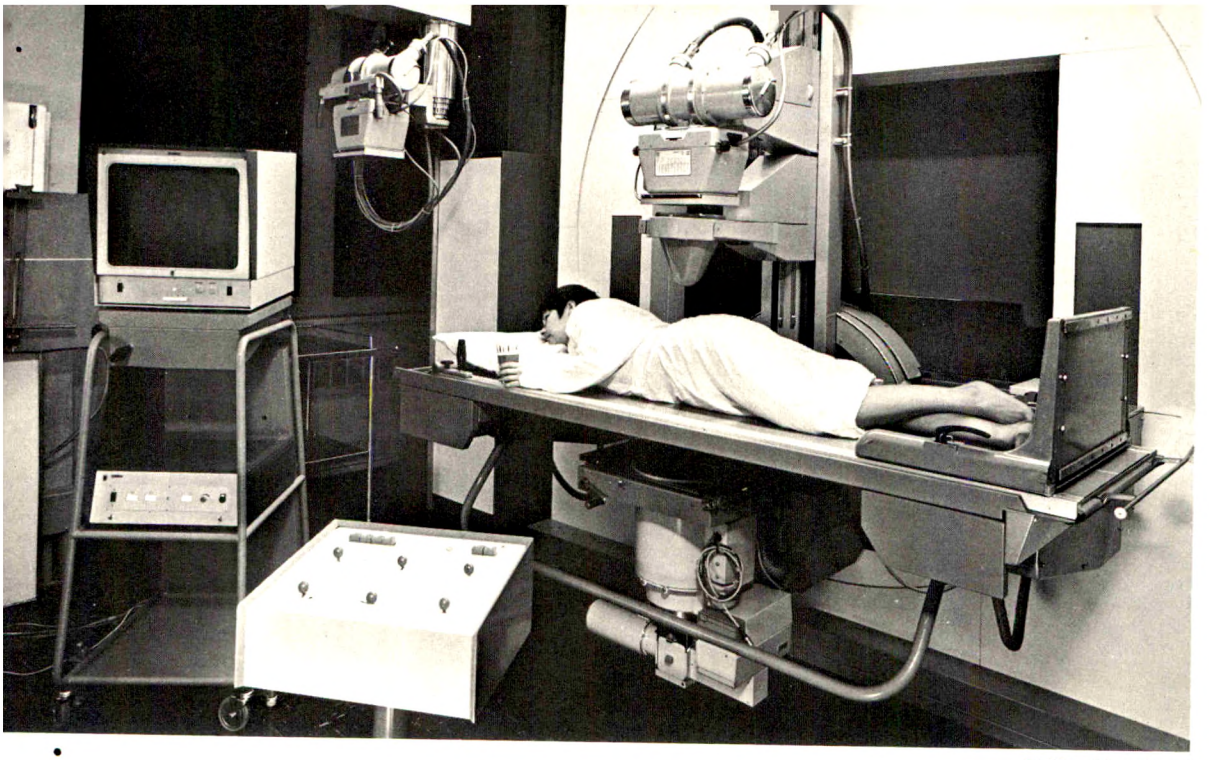


Why PHILIPS IMAGE INTENSIFIER SYSTEMS are synonymous with Quality X-ray Performance



Many new examination techniques, such as heart catheterization depend heavily on electro-optical performance of intensifiers. By providing a brighter, clearer x-ray image — the Philips image intensifiers allow most effective use of TV, cine and 70 mm spot-films for diagnostic information gathering and storage.

As pioneers in the design and development of radiographic imaging systems, we ensure superior performance by seeing to it that superior manufacturing standards are carried out with exacting care.



Philips Ring Stand

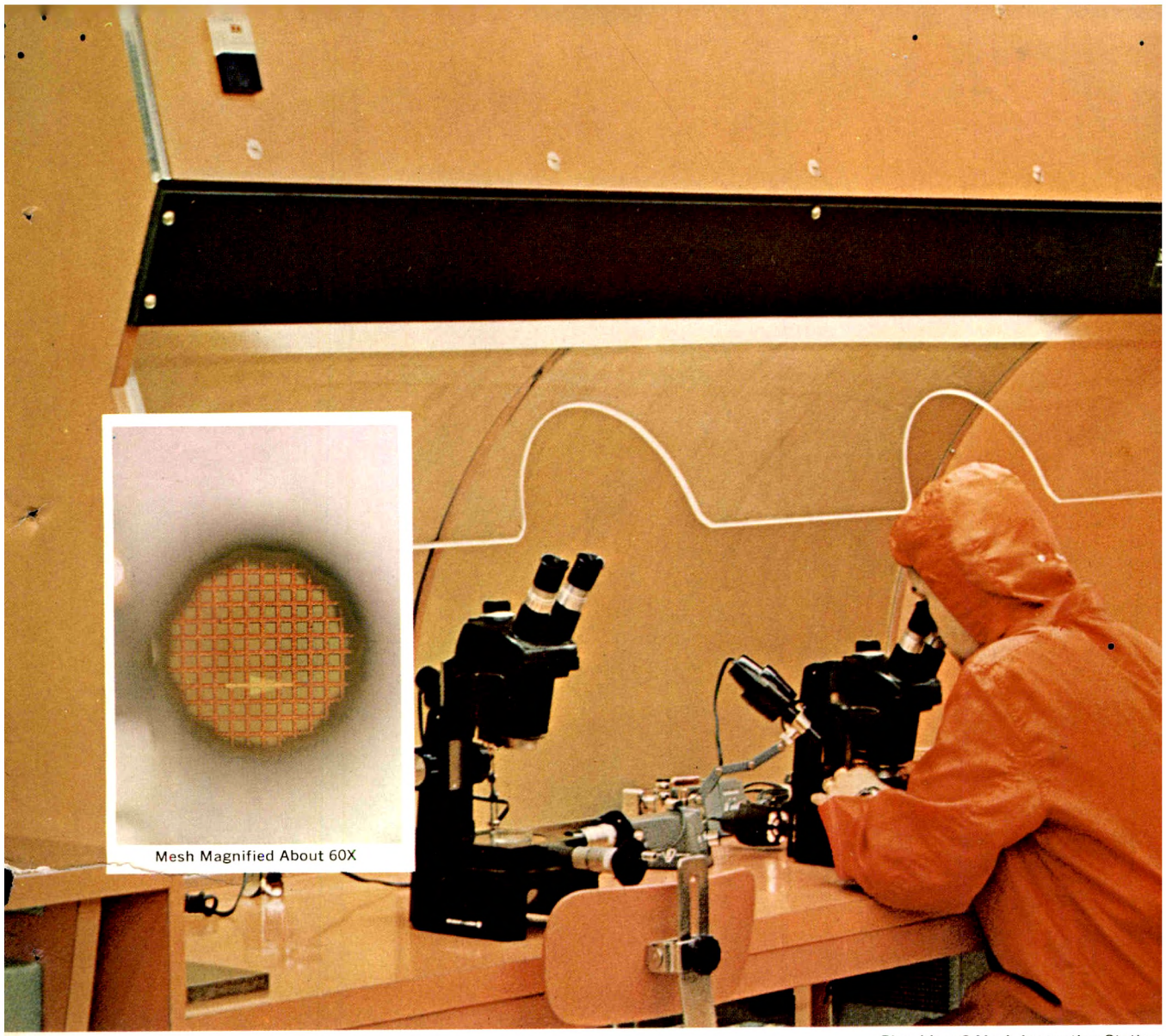
Quality Performance Begins with Design, Is Perfected in Manufacture and Testing

For example, ½ micron of dust on an image intensifier phosphor could create misleading artifacts or distortion on a radiograph. Therefore, Philips image intensifiers are manufactured in these Class 100 "super-clean" rooms — employing design features and equipment unduplicated in the industry. This is only one example of quality control carried out in manufacture by our wholly owned subsidiary, Amperex Electronic Corporation, at Slatersville, R.I.

In fact, the new plant has been specially constructed to assure utmost manufacturing precision and cleanliness in image intensifier tube and Plumbicon TV camera tube production. Here, every step, followed by testing, re-testing, is rigorously controlled. The result is quality performance, economy and long life in a superior imaging system.

Forming Glass Envelope for X-ray Image Intensifier

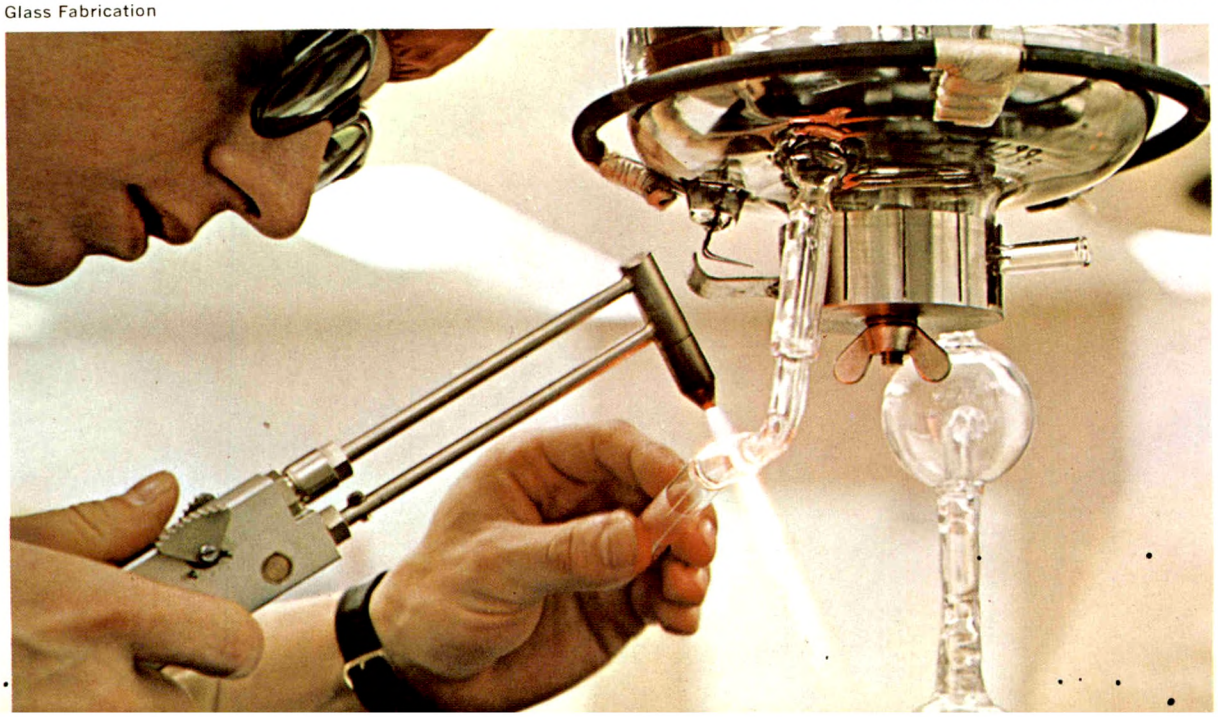


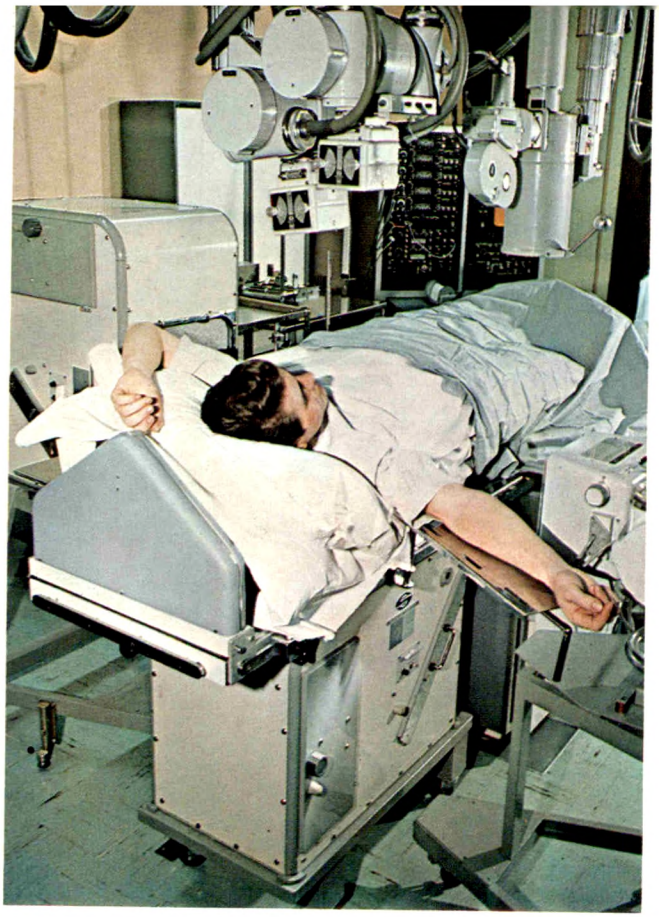


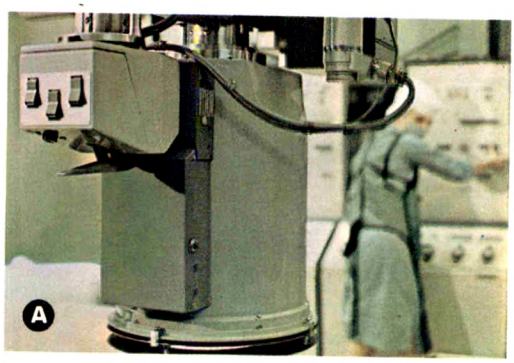
Mesh Magnified About 60X

Plumbicon® Mesh Inspection Station

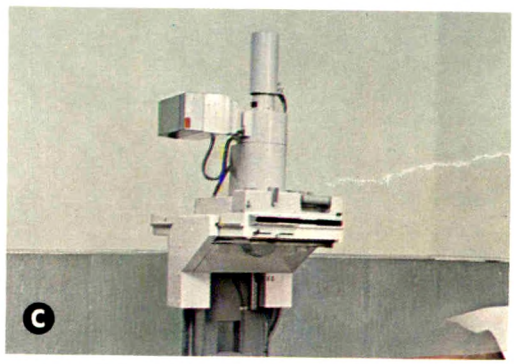
Glass Fabrication

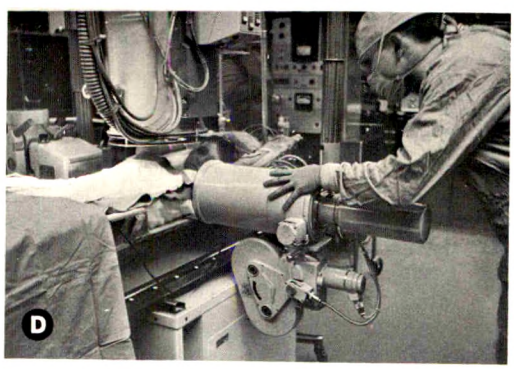












M-158

Systems Engineering — Key to Flexibility, Compatibility

The Philips Image Intensifier, heart of a number of sophisticated equipment systems, is completely integrated in design and manufacture. All elements were designed in conjunction with one another to assure maximum compatibility.

Use television or direct observation. Use videotape recorders. Use 16 mm or 35 mm cine, 70 mm spotfilm radiography. Use them singly or in combination. Our systems are flexible enough to meet your needs. And, modular design features ensure ease of maintenance and adaptability.

(A) Philips 6″ or 9″/5″ Image Intensifiers are adaptable to every situation — from routine radiography to biplane myelography and stereo heart catheterization techniques.

(B) Convenient TV permits image-brightened viewing and freedom of movement for radiology teams. Motion phenomena observed on TV, can be recorded on videotape for instant playback, or later study and teaching.

(C) The 70 mm spotfilm camera provides sharp diagnostic films. Rapid 6 per second sequencing permits instant radiography of motion phenomena.

(D) Image-intensified 16 and 35 mm cine offers a practical means to record dynamic studies which are easily retrieved for diagnostic review or education.

Plumbicon is the registered trademark of NV Philips for television camera tubes.

PHILIPS MEDICAL SYSTEMS

North American Philips Company, Inc., New York 10017

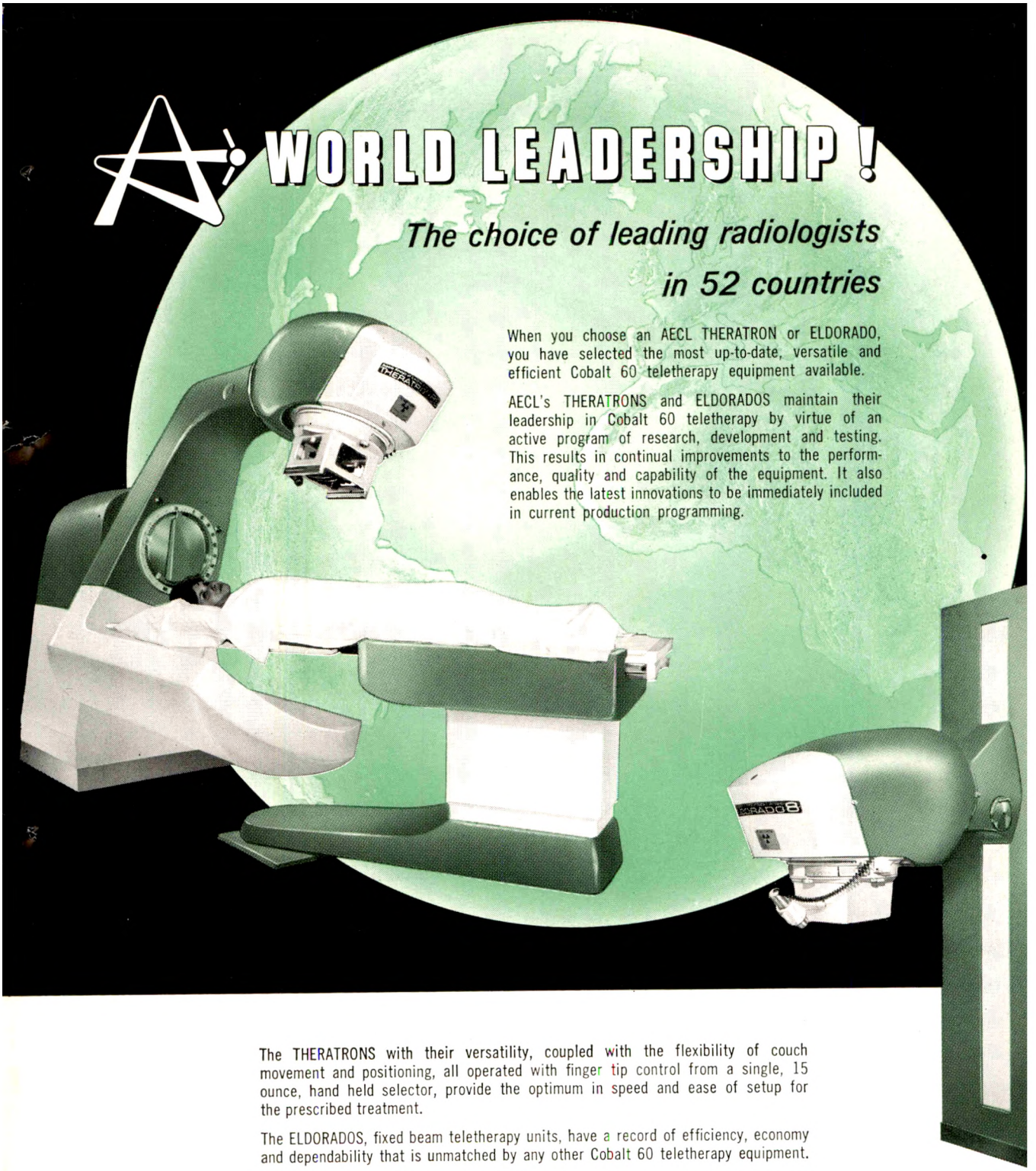
As of December 1, 1968, the Norelco Medical Division is to be known as the Medical Systems Division of North American Philips Company, Inc.

WORLD LEADERSHIP !

The choice of leading radiologists in 52 countries

When you choose an AECL THERATRON or ELDORADO, you have selected the most up-to-date, versatile and efficient Cobalt 60 teletherapy equipment available.

AECL's THERATRONS and ELDORADOS maintain their leadership in Cobalt 60 teletherapy by virtue of an active program of research, development and testing. This results in continual improvements to the performance, quality and capability of the equipment. It also enables the latest innovations to be immediately included in current production programming.



The THERATRONS with their versatility, coupled with the flexibility of couch movement and positioning, all operated with finger tip control from a single, 15 ounce, hand held selector, provide the optimum in speed and ease of setup for the prescribed treatment.

The ELDORADOS, fixed beam teletherapy units, have a record of efficiency, economy and dependability that is unmatched by any other Cobalt 60 teletherapy equipment.

AECL's WORLD LEADERSHIP in Cobalt 60 teletherapy is the result of a long record of **proven performance.** World wide representation provides immediate service — anywhere! For detailed information please write to the address below.

Atomic Energy of Canada Limited

Commercial Products

68.3M

P.O. Box 93, Ottawa, Canada • Tel. 836-2790 • Area Code 613 • Cable 'NEMOTA'



Barnes-Hind Barium Products
Subsidiary of Barnes-Hind Pharmaceuticals, Inc.
Sunnyvale, Calif. 94086

The no-mix.

We took the construction work out of barium sulfate.

We premixed it into a smooth, creamy, instantly ready esophageal contrast medium.

Before, coating was often a hit-or-miss operation ('home-brewed' barium can be too thin, too thick or just plain settled out).

Not anymore.

Now, in seconds, you can photograph your patient's esophageal tract...easily take 3, 4, even 5, plates after an initial dose. In many patients the coating of Esophotrast lasts up to 15 minutes (ample time for fluoroscopy and radiography of the esophagus and evaluation of heart size).

Now you don't have to cajole your patients into drinking cupful after cupful of barium...the 1 oz. of Esophotrast, usually all that's needed, is nongritty and fruit-flavored–a really pleasant medium to take.

And it's just a squeeze of a tube away.

So why mix your own?

Esophotrast®

(barium sulfate)

Instantly ready esophageal cream

Recommended dose: 1 tablespoonful "chewed" thoroughly before swallowing. Repeat with a second tablespoonful to ensure prolonged adherence and coating of the esophageal mucosa.

- X-RAY MACHINE
- X-RAY TUBE
- FILTERS, CONES, AND APERTURE DIAPHRAGMS
- PATIENT
- DISTANCE
- GRIDS
- INTENSIFYING SCREENS
- X-RAY FILM
- PROCESSING
- FOG (ALL FORMS)
- VIEWING CONDITIONS



Any of these 11 factors can affect diagnostic clarity.

Du Pont has a new training seminar for resident radiologists that discusses each one.

This Du Pont seminar, entitled "Factors Affecting Diagnostic Clarity," is now being conducted in teaching hospitals across the country.

It demonstrates, with over 150 original radiographs, how the factors on the opposite page affect density, contrast, detail and distortion.

Residents tell us the seminar provides a better understanding of the radiographic process. It enables them to communicate more effectively with technologists.

We believe this seminar can be a meaningful supplement to the education of a radiologist. It results in better communication, fewer re-examinations and improved diagnostic clarity.

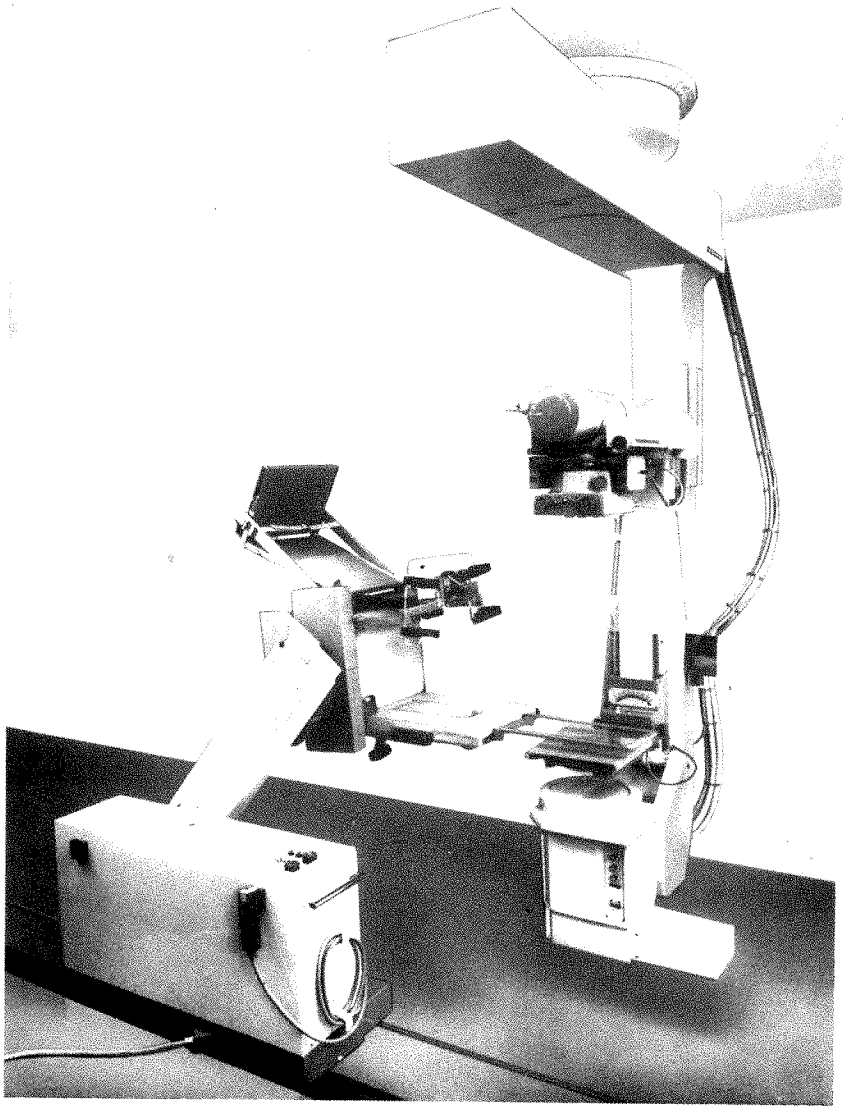
Training seminars are an important facet of Du Pont's focus on diagnostic clarity. Why not take advantage of them? Teaching institutions are invited to schedule this resident program through their Du Pont Technical Representative.

DU PONT REG. U.S. PAT. OFF. **CRONEX® X-ray Products**

MIMER III

NEURORADIOLOGICAL UNIT

WITH RCT-2 ROTATING CHAIR



Examinations:

Pneumo-encephalography
Ventriculography
Gas myelography
Cerebral angiography

Techniques:

TV-Fluoroscopy
Laminography
Magnification
Standard radiography

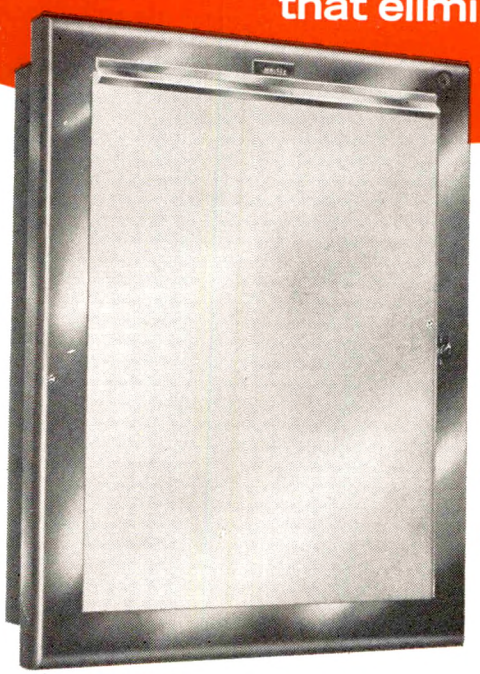
ELEMA-SCHONANDER, INC., P.O. BOX 130, MT. PROSPECT, ILL. 60056
Tel. (312) 259-7206



Better looking . . . and better, safer viewing!

HALSEY STAINLESS STEEL ILLUMINATORS

Sleekly beautiful – and now with meter-tested light distribution, plus new safety cord set that eliminates shock hazards



No. 250-I-R-IG — recessed; with Instant-Grip. Gracefully rounded frame flows smoothly into the wall when illuminator is recessed.

- **Photometer-tested lighting** assures even light distribution
- **Improved P-80 plexiglas** front panel has ground-glass finish on its inner surface, providing 20% better illumination on the film
- **Easily removable front panel,** for easy lamp replacement
- **"Invisible" welds** improve appearance, eliminate hazard of sharp corners projecting from wall or desk
- **New 3-wire U-ground cord set** with lock-in grommet and molded plug protects fully against danger of shock
- **Listed with UL Laboratories** — Guide No. 480E0

No. 250-I-R-IG. Recessed model with Instant-Grip
No. 250-I-R. Recessed model with 2-way film clips
No. 250-I-IG. Desk model with Instant-Grip
No. 250-I. Desk model with 2-way film clips

Write for literature on the complete Halsey illuminator line

Through your dealer

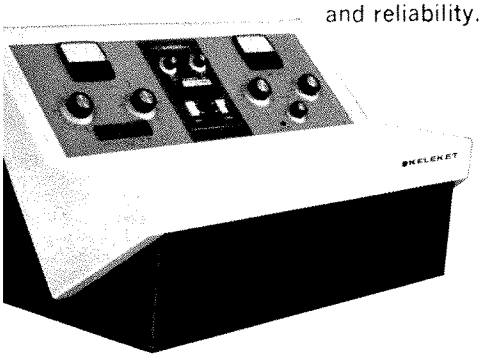
HALSEY X-RAY PRODUCTS, INC.
1425-37th STREET, BROOKLYN, N.Y. 11218

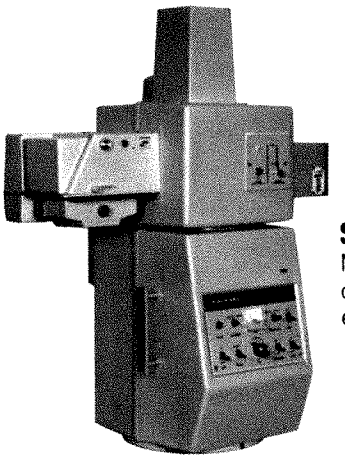
CHICAGO: 7321 Monticello Avenue, Skokie, Illinois

HALSEY

New and improved products... expanded technical support

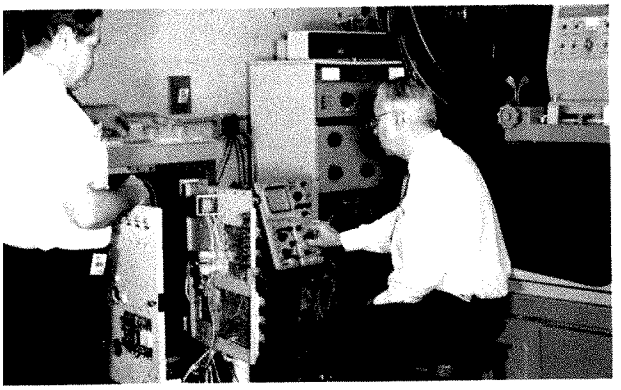
HARLECH 240
The original solid state x-ray generator with field proven quality and reliability.

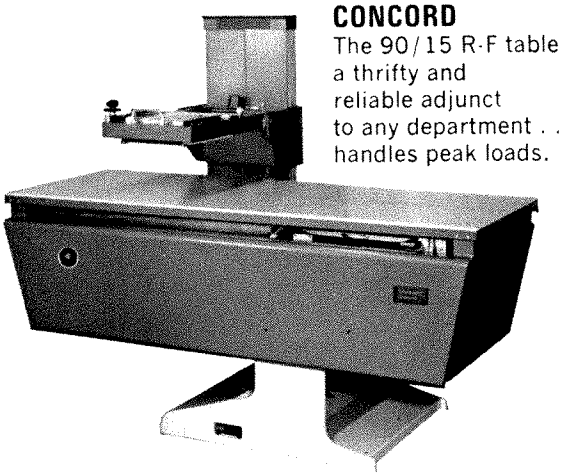




SCAT V
New optical design for image enhancement.

ADVANCED ENGINEERING LAB
Where the ideas of today become tomorrow's products for improved diagnosis.



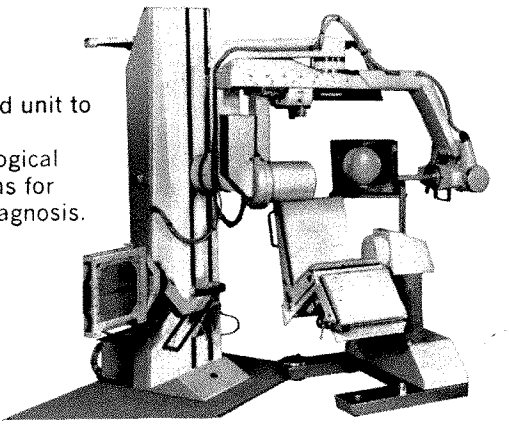


CONCORD
The 90/15 R-F table . . . a thrifty and reliable adjunct to any department . . . handles peak loads.

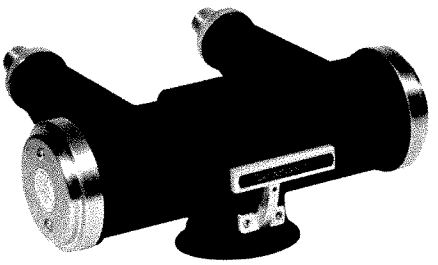
NIMO-70
The 70 mm spot film camera adaptable to our NIMO, the nine inch intensifier system with mirror optics.



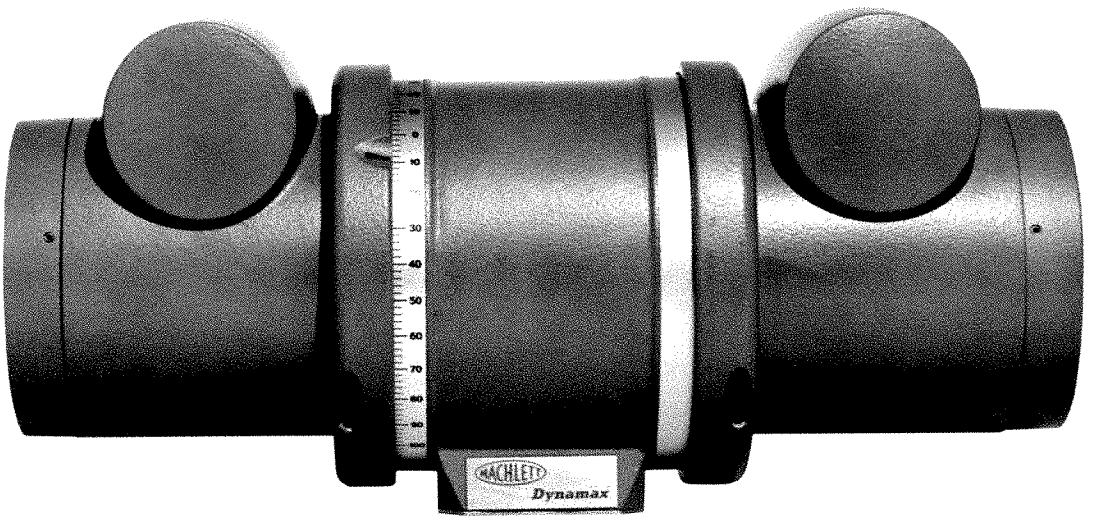
PRINCEPS
A specialized unit to perform all neuroradiological examinations for complete diagnosis.



KELEKET CGR



If your x-ray tube
was this big in 1960,



it should be this big in 1969
to keep pace with the growing work load
of your x-ray department.

MACHLETT

MACHLETT

Although your present x-ray tube was undoubtedly adequate to meet your original requirements, it is quite possible that today this x-ray tube is often overloaded as a result of increased exposure frequency. Stepped-up numbers of examinations and films per study, together with markedly shortened film processing times, create a condition which requires greater x-ray tube capacity.

■ Anticipating this escalation in x-ray exposures, Machlett has increased the thermal capacity of all rotating anode x-ray tubes, from the Dynamax "HD25" to the Dynamax "HD50". In addition, the larger, higher rated tubes such as the Dynamax "60" and Dynamax "61" have been made available.

■ Machlett is prepared to assist you in selecting the x-ray tube most adequate for today's work loads. Consult your x-ray dealer or write to The Machlett Laboratories, Inc., to determine which Dynamax rotating anode x-ray tube best meets your needs.



THE MACHLETT LABORATORIES, INC., 1063 Hope Street, Stamford, Connecticut 06907.

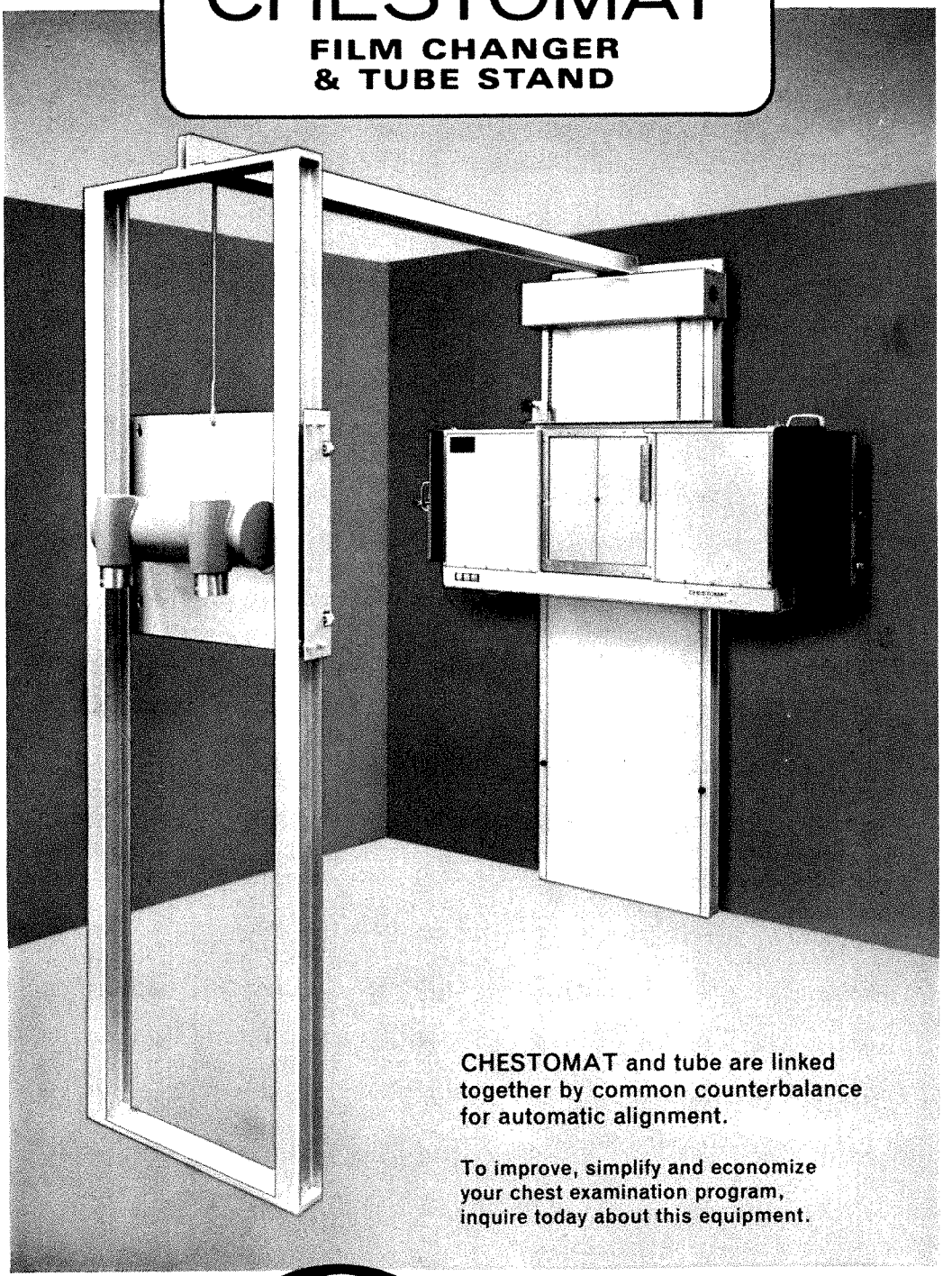
RAYTHEON

THE MACHLETT LABORATORIES, INC.

A SUBSIDIARY OF RAYTHEON COMPANY

CHESTOMAT

FILM CHANGER & TUBE STAND



CHESTOMAT and tube are linked together by common counterbalance for automatic alignment.

To improve, simplify and economize your chest examination program, inquire today about this equipment.

SCHICK X-RAY

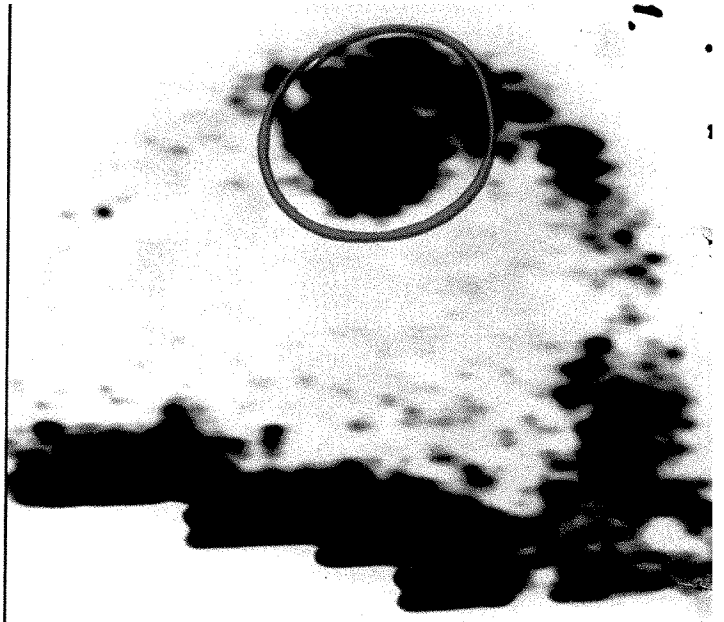
SCHICK X-RAY CO., INC.

415 Green Bay Road • Wilmette, Illinois 60091

Phone (312) 256-4700



POSTERIOR R



LEFT LATERAL

In suspected brain pathology, find out fast with **Pertscan**-99m

For brain scanning, Pertscan-99m provides more information with less radiation to the patient than any other related cerebral test—whether other radioisotopes or x-rays. And you get each projection fast—as little as 2 minutes with a camera, 15 minutes or less with rectilinear scanners.

A 54-year-old man was hospitalized with progressive weakness of the right side, followed by seizures of the right side (Jacksonian seizures). Brain scans showed an abnormal concentration of isotope in the left parasagittal area. Surgery revealed a meningioma, which was removed, and the patient recovered.

The 2 scans above, showing the marked abnormal uptake (which turned out to be a menigioma), were made with Pertscan-99m. This product is shipped Monday through Friday—and Sunday. Thus, brain scans can be scheduled 6 days a week—Monday through Saturday.

INDICATIONS: Adjunctive diagnostic aid in detecting and localizing intracranial neoplastic (primary or metastatic) and non-neoplastic lesions.

CONTRAINDICATIONS: Radio-pharmaceutical agents should not be administered to pregnant women or to persons less than 18 years old unless the indications are very exceptional.

PRECAUTIONS: Care should be taken to ensure minimum radiation exposure to the patient as well as all personnel; to prevent extracranial contamination because this can lead to erroneous interpretation; and to differentiate areas of abnormal activity from areas of normal vascular activity.

Pertscan™-99m
SODIUM PERTECHNETATE Tc 99m

Also available:

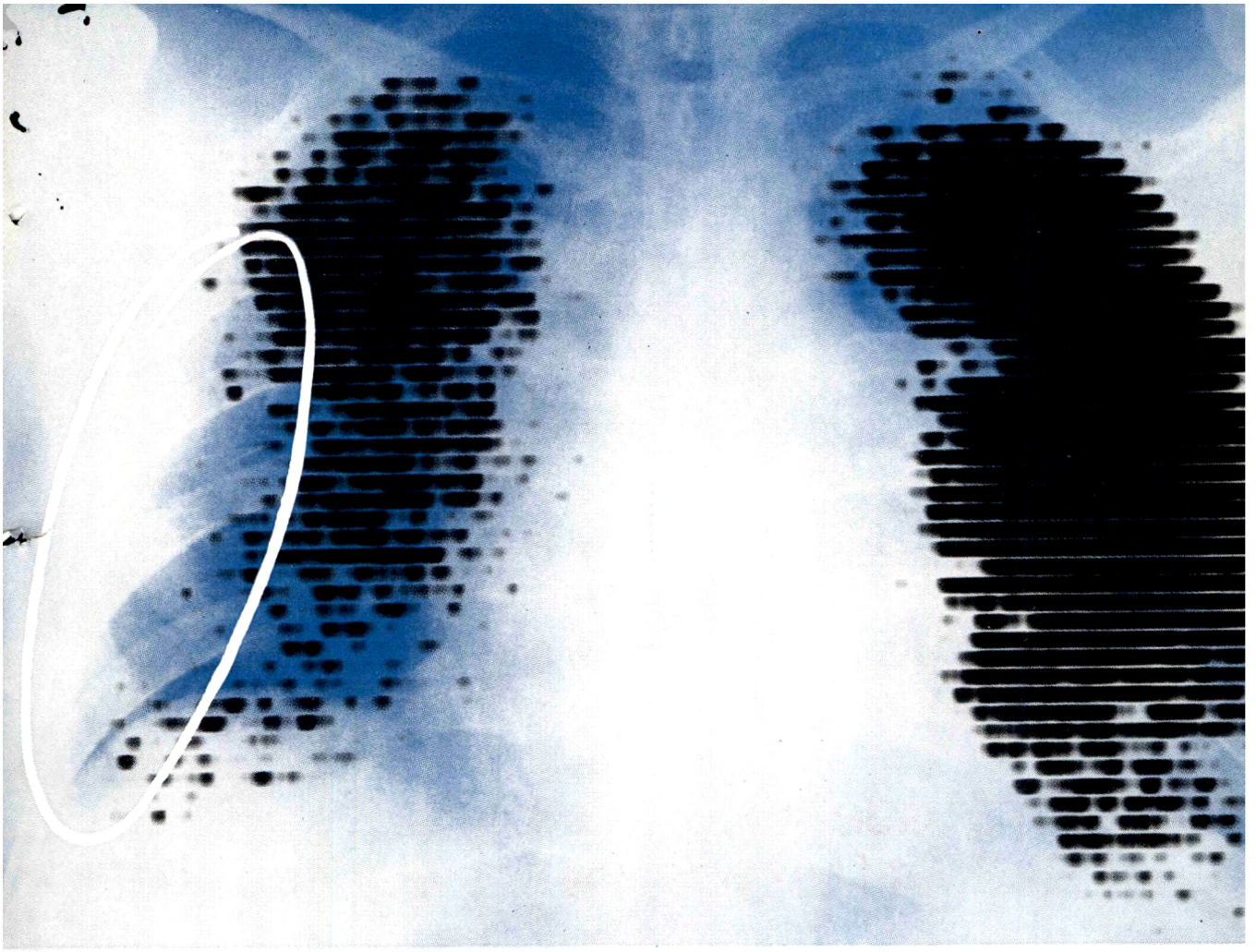
Pertgen™-99m
TECHNETIUM 99m GENERATOR KIT

ABBOTT LABORATORIES NORTH CHICAGO, ILLINOIS

Abbott Laboratories, S.A., 2, rue Thalberg, 1201 Geneva, Switzerland

TM—Trademark

804464



If it's a pulmonary problem, **Macroscan-131** pictures i

A 50-year-old man was hospitalized after complaining of vague chest pains. Shortly after, he suffered a cardiac arrest. An EKG showed no evidence of cardiac infarction. A lung scan revealed a decreased concentration of isotope in the right lower lobe. This was diagnosed as a pulmonary infarct, therapy was instituted, and the patient recovered.

His scan above, showing the marked diminished uptake, was made with Macroscan-131. This product has many diagnostic uses:

Pulmonary embolism, suspected: To confirm (or rule out) its occurrence.

Chronic pulmonary tuberculosis: To estimate unilateral and regional function and perfusion of the lungs.

Emphysema: To evaluate the decreased regional blood flow that occurs with obstruction of vessels.

Pneumonitis: To evaluate the decreased regional blood flow that occurs without obstruction of vessels.

Lung Tumors: To evaluate the regional ischemia resulting from compression or obstruction of pulmonary arteries.

Surgery and/or other therapy for lung disorders: To evaluate the effectiveness of therapeutic meas ures.

Macroscan-131 is sterile and non-pyrogenic. It i ready to use and should not be heated prior to use

INDICATIONS: For scintillation scanning of the lungs t evaluate total, unilateral, and regional arterial perfusic of the lungs.

CONTRAINDICATIONS: Radio-pharmaceutical agen should not be administered to pregnant women or to pe sons less than 18 years old unless the indications a very exceptional.

PRECAUTIONS, SIDE EFFECTS: Care should be taken administer the minimum dose consistent with safety ar validity of data. The possibility of an immunological r sponse to albumin should be kept in mind when seri scans are performed. There is a theoretical hazard acute cor pulmonale, because of the temporary small ac ditional mechanical impediment to pulmonary blood flo A possible case of urticaria has been related to a similar preparation. The thyroid gland should be protected by prophylactic administration of concentrated iodide solution.

Macroscan™-13

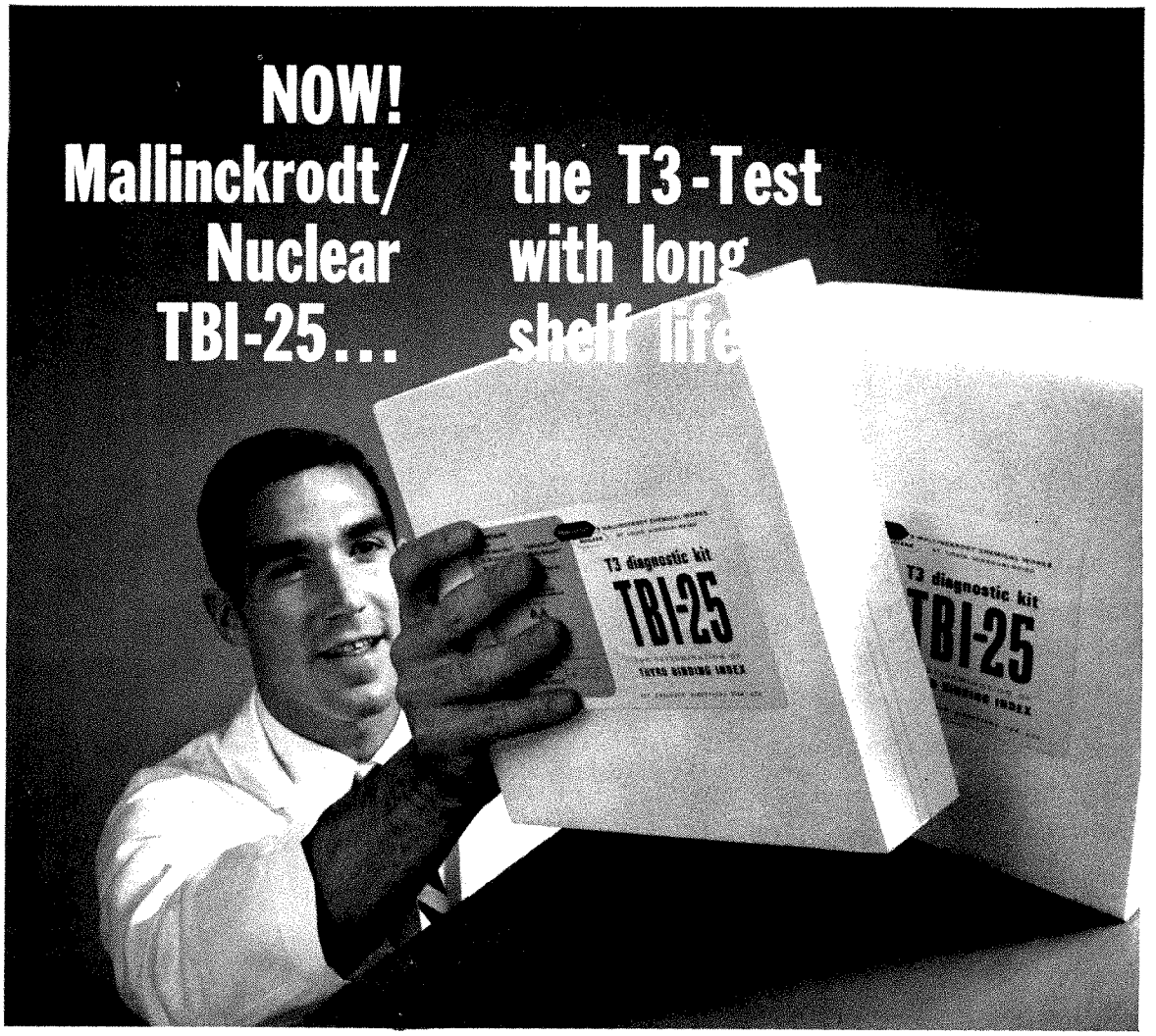
AGGREGATED RADIO-IODINATED (I^{131}) ALBUMIN (HUMAN

ABBOTT LABORATORIES NORTH CHICAGO, ILLINOIS

TM—Trademark.

Abbott Laboratories, S.A., 2, rue Thalberg, 1201 Geneva, Switzerland

80



TBI-25, with iodine-125, is the T-3 test of choice that you can use now or a month from now. Stock it today. It's ready when you need it.

TBI-25 and TBI . . . Your Choice
TBI-25 with iodine-125 and TBI with iodine-131 are both available to meet your individual T-3 requirements. The TBI family, with direct measurement of binding site uptake, offers a high degree of accuracy and takes less technician time. Write for full information and new TBI booklet.

Mallinckrodt®
NUCLEAR

RADIOPHARMACEUTICALS
MALLINCKRODT CHEMICAL WORKS
Box 10172 • Lambert Field
St. Louis, Missouri 63145
Atlanta • Chicago • Cleveland
Los Angeles • New York • Montreal

*See our other new products at the **RSNA** meeting*

SIEMENS

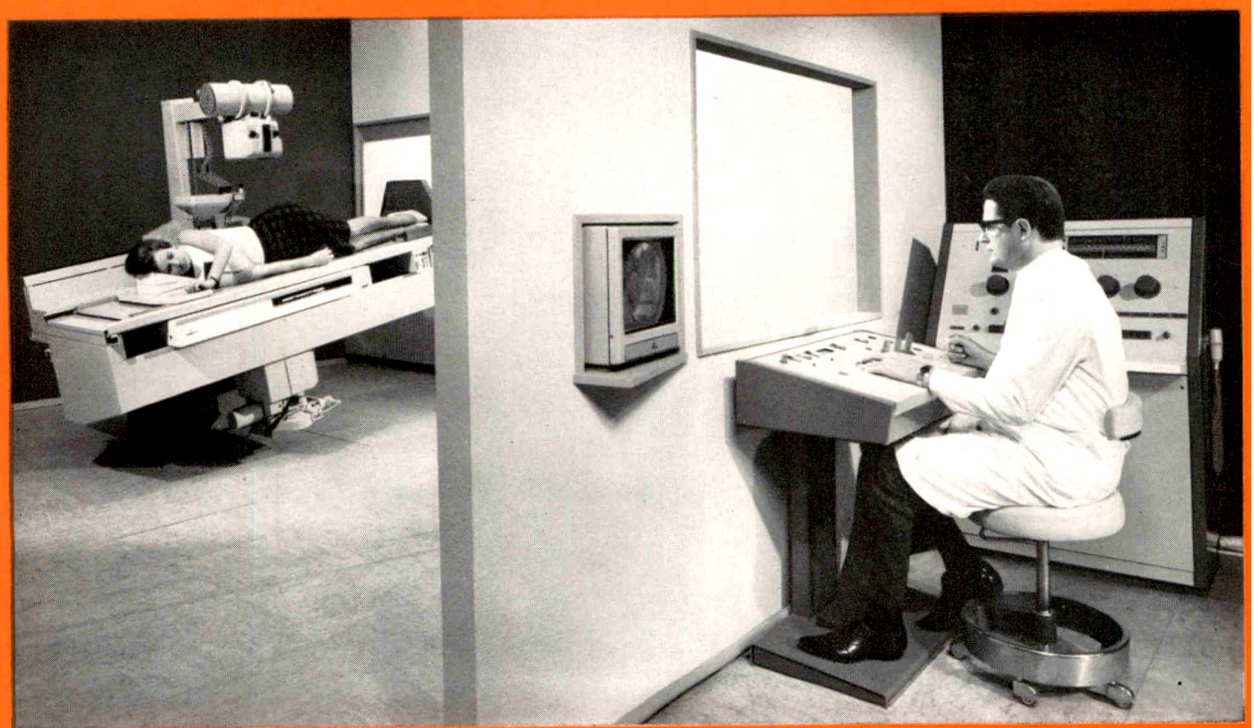
SIREGRAPH System Approach

From its remote control console to the smallest table accessory, the SIREGRAPH is the „System Approach" to the radiologists' most pressing problems – how to obtain the highest possible consistent quality of information and how to make the most efficient use of his time.

Outstanding features include:

- 90/90 continuously variable speed motor driven tilting table
- Rotating cradle (optional)
- Two way power top
- Fully automatic undertable spot film device for use with five various cassette sizes
- Built-in 10/6 SIRECON Image Intensifier with television which tracks the X-ray beam through all angulations of X-ray tube or table
- Routine and special techniques including planigraphy and zonography
- Choice of recording methods from image system 70 – 35 mm or 16 mm cine

SIEMENS MEDICAL OF AMERICA INC.
685 LIBERTY AVENUE, UNION, N.J. 07083



We are unwrapping a new, completely interchangeable, 90-second film.

New FINEX* II.

Can be used for all processing systems, automatic as well as manual. Requires no changes in exposure. Medium speed. Extra-fine grain. Polyester base. Perfect complement to GAF-X™ film. Choose from a complete line of 90-second x-ray films.

See your GAF representative for the proof.

GAF Corporation
(Formerly General Aniline & Film Corporation)
140 West 51 Street, New York, New York 10020

FINEX* II

medical x-ray film

another fine product from gaf®

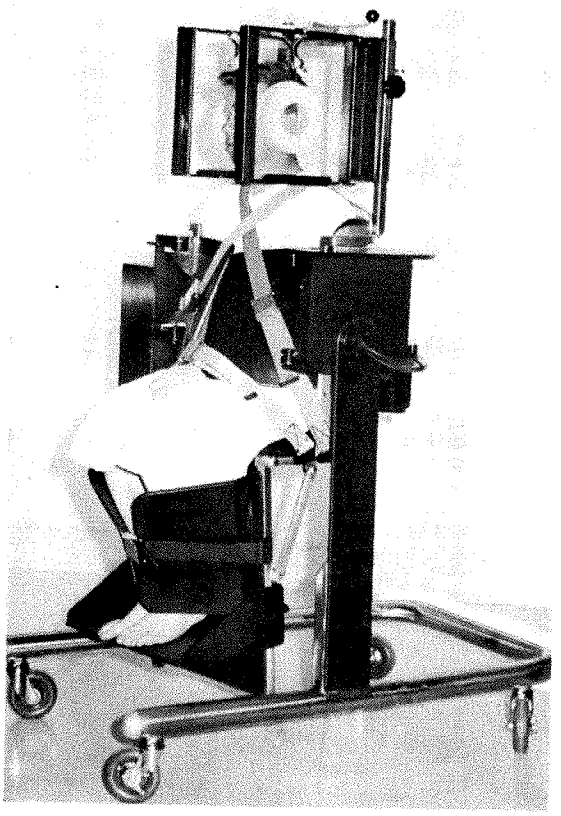
* Trademark of GAF Corporation

12668-1000

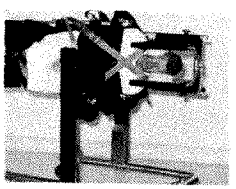

gaf
gaf

AMPLATZ

Pneumotomographic Chair



CHAIR SHOWN IN UPRIGHT POSITION



CHAIR SHOWN IN LEFT LATERAL DECUBITUS POSITION



CHAIR SHOWN WITH INFANT SEAT ATTACHED

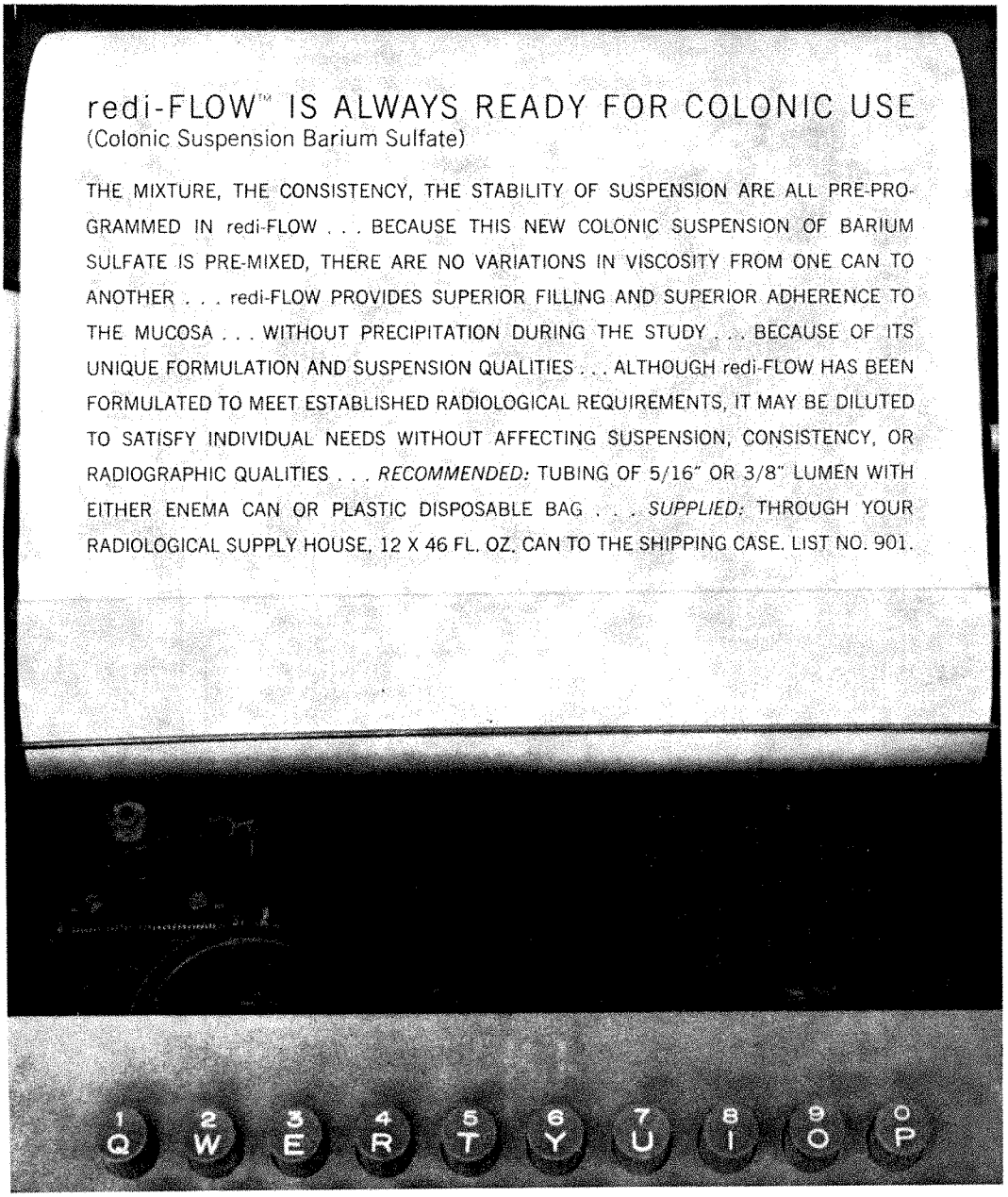
A versatile fully motorized chair for pneumoencephalography and remotely controlled autotomography. Lumbar punctures and pressure measurements are easily accomplished in upright or decubitus position thru the window in back of chair while the patient is safely immobilized.

Patient's head is held securely and comfortably by polyurethane cushions and specially designed transparent head holders eliminating rotated radiographs. Upright, brow-up and brow-down positions in addition to somersault rotation, is accomplished by motor or manual drive. With the specially designed motorized gear system, the patient can be placed into the right and left decubitus position for temporal horn studies.

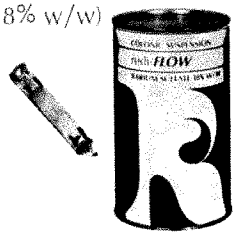
Autotomography in AP, PA, or lateral projections can be carried out in any position by remotely activating vibration-free power drive, eliminating exposure to x-ray personnel. (Additional removable cassette holders are provided for AP or lateral tomograms. The entire holder is vertically adjustable for 7½").Any size patient can be accomodated by the seat and head holder adjustments. The infant seat, which is included, can be simply attached.

NEDMAC, INC. MEDICAL INSTRUMENTS DIVISION
SCIENCE INDUSTRY CENTER 5410 INTERNATIONAL PARKWAY
MINNEAPOLIS, MINNESOTA 55428 U.S.A.

NATIONWIDE DISTRIBUTION THROUGH X-RAY DISTRIBUTORS



redi-FLOW
(colonic suspension
barium sulfate
18% w/w)



write for samples:

FLOW PHARMACEUTICALS, Inc.

Subsidiary of Flow Laboratories, Incorporated
Mountain View, California 94040

™ redi-FLOW is a trade mark of Flow Pharmaceuticals, Inc.

Also available: redi-FLOW gastric suspension barium sulfate 30% w/w: Always ready for use, always uniform in consistency, always in stable suspension, always reproducible results, always a fresh flavor taste, always a high level of patient acceptance.

The Slippery One.

There are lots of overhead tube conveyers around today. But not like this one. Go ahead, try it. Pull it all the way down. Take a finger and raise it back. Walk it around.

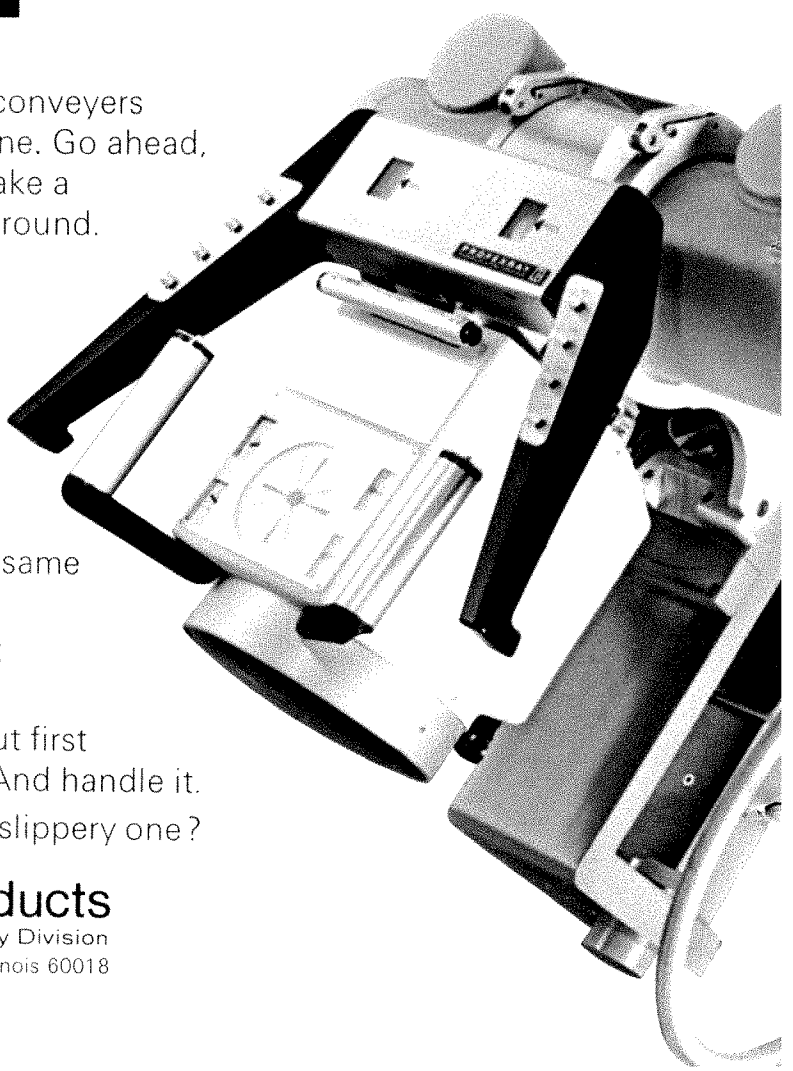
See? Not a hitch.

That's why we call it the slippery one. Because these mechanisms have been perfected. Then polished. Then perfected again. Until working with them is not just satisfactory—but satisfying. The same as with all Profexray equipment.

We think that makes our product better than anybody's.

We'd like you to think so, too. But first you'll have to see it. And feel it. And handle it.

How soon can we show you our slippery one?



Litton Medical Products
A Litton Industries Group, Profexray Division
515 East Touhy Avenue—Des Plaines, Illinois 60018


PROFEXRAY

CLEAR CHOICE IN HYSTEROSALPINGOGRAPHY

WATER-SOLUBLE CONTRAST MEDIUM

SALPIX®

0.53 Gm Sodium Acetrizoate and 0.23 Gm Polyvinylpyrrolidone per cc

Fast, safe, accurate radiopaque visualization without irritation, residue, or pain

Ortho

ORTHO PHARMACEUTICAL CORPORATION • RARITAN, NEW JERSEY

CONTRAINDICATIONS—Contraindications to hysterosalpingography include the presence of severe vaginal or cervical infections, existing or recent pelvic infection, marked cervical erosion or endocervicitis, and pregnancy. The procedure is contraindicated during the immediate pre- or post-menstrual phase. SENSITIVITY—If indicated in the patient's history, an intracutaneous skin test or sublingual absorption observation may be done with 0.1 cc SALPIX. WARNING—Not for intravenous use.

©OPC 1966



3 WAYS to OPTIMUM LAB EFFICIENCY

Make certain these books are available to every technologist in your lab

1 *New 3rd Edition!* **PATIENT CARE AND SPECIAL PROCEDURES IN RADIOLOGIC TECHNOLOGY,** *by John C. Watson, R.T.* This practical book gives the technologist the latest information on specifics of patient care, plus practical, technical help on performing many special x-ray procedures. Includes vital new material on the image intensifier and its use in fluoroscopy; zonography; magnification x-ray techniques; proper techniques for withdrawing contrast media from an ampule or rubber-stopper vial; advantages of the CircOlectric bed. January, 1969, approx. 248 pages, 146 illustrations, **about $8.25.**

2 *New 4th Edition!* **TEXTBOOK OF RADIOLOGIC TECHNOLOGY,** *by Charles A. Jacobi, B.Sc., R.T.(A.R.R.T.); and Don Q Paris, R.T.(A.R.R.T.).* For review of specialized procedures or for quick answers to questions arising in any area of the technologist's responsibility. In a step-by-step outline format, surveys fundamentals of physics, chemistry, anatomy and physiology, as well as positioning techniques, plus "technical tips" from the authors' experience. August, 1968, 499 pages, 384 illustrations, **$12.75.**

3 *New!* **TEXTBOOK OF ANATOMY AND PHYSIOLOGY IN RADIOLOGIC TECHNOLOGY,** *by Charles A. Jacobi, B.Sc., R.T.(A.R.R.T.).* Relates anatomy and physiology to practical, everyday radiologic technology. Provides the technologist with a straightforward correlation of anatomy with such current techniques as teleroentgenography. Uses BNA and NA terminology and actual skeleton photographs. April, 1968, 439 pages, 187 illustrations, **$12.00.**

— — —THE C. V. MOSBY COMPANY
3207 Washington Boulevard

MOSBY

Publishers— — —
St. Louis, Mo. 63103

Please send me the book(s) indicated on 30-day approval. At the end of this time I may either keep it (them) and forward my payment or return the book(s) without charge or obligation. I understand that I can save delivery charges by enclosing remittance with this order—the same return privilege is guaranteed.

☐ Payment enclosed (same return privilege)

☐ Bill me

30-day approval offer good only in Continental U.S. and Canada

☐ Watson, PATIENT CARE AND SPECIAL PROCEDURES IN RADIOLOGIC TECHNOLOGY, 3rd edition, about $8.25

☐ Jacobi-Paris, TEXTBOOK OF RADIOLOGIC TECHNOLOGY, 4th edition, $12.75

☐ Jacobi, TEXTBOOK OF ANATOMY AND PHYSIOLOGY IN RADIOLOGIC TECHNOLOGY, $12.00

NAME _____

HOSPITAL OR LABORATORY _____

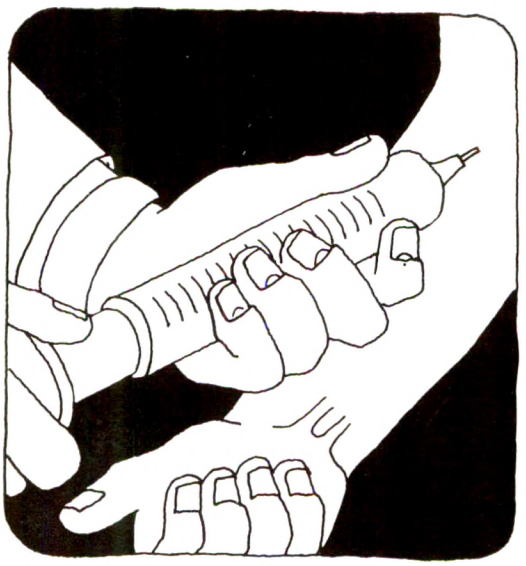
ADDRESS _____

CITY _____

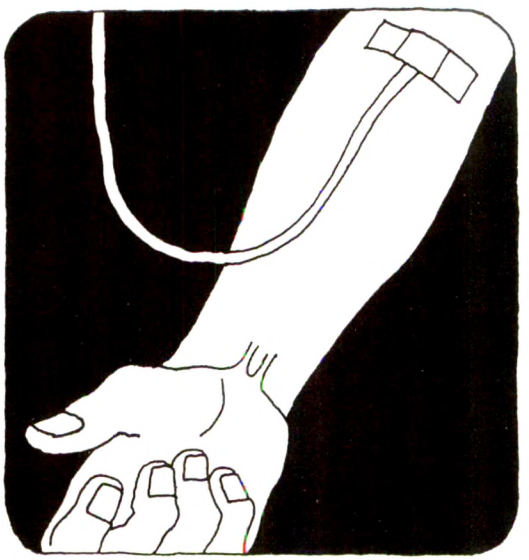
STATE _____ ZIP _____

ARRN-1-69

Now...2 important I.V. Radiodiagnostic procedures for improved visualization



Adequate Dose Urography
with 50-60 ml. of 50% solution



Drip Infusion Pyelography
using between 250-400 ml. of a 25% solution*

with Hypaque® Sodium 50%

brand of sodium diatrizoate Sterile Aqueous Solution

Winthrop

PIONEERS IN PRODUCTS FOR RADIOLOGIC DIAGNOSIS

*By diluting the 50% solution with an equal amount of sterile water for injection, USP, sodium chloride injection, USP, or dextrose injection, 5%, USP.

(Please see summary on following page)

Hypaque® 50%

sodium

brand of **sodium diatrizoate**

Sterile Aqueous Injection

(Weight/Volume)

Excretory Urography and Drip Infusion Pyelography

Description: Hypaque sodium is sodium 3,5-diacetamido-2,4,6-triiodobenzoate, a radiopaque medium used to delineate internal structures.

Warning: Do not use Hypaque sodium for myelography. Injection of even a small amount into the subarachnoid space may produce convulsions and result in fatality.

General and Specific Precautions: Caution is advised in patients with a history of bronchial asthma, other allergic manifestations, or of sensitivity to iodine; these conditions represent a special risk, though not an absolute contraindication. To avoid or minimize possible allergic reactions, premedication with antihistamines may be considered. Benadryl (diphenhydramine hydrochloride) in the same syringe with Hypaque may result in precipitation. A test dose of contrast medium is not entirely reliable. Severe reactions, including fatalities, have occurred with a test dose as well as with the full diagnostic dose.

Caution is advised in patients with severe cardiovascular disease. In patients with impaired renal function and cardiovascular disease, drip infusion pyelography imposes a sudden osmotic and sodium load which can precipitate congestive heart failure. Contrast media injected into arteries or veins can promote sickling of red cells in susceptible individuals. In patients with reduced renal function, repeat of excretory or retrograde pyelography should be delayed at least 48 hours to avoid temporary suppression of urine. In preparation for excretory urography of patients with multiple myeloma, partial dehydration is not recommended, since this may predispose to the precipitation of myeloma protein in the kidney tubules. When thyroid function studies (PBI and 24-hour radioiodine uptake levels) are indicated, they should be performed *prior* to radiographic studies or several days afterwards, to avoid inaccurate results.

Hypaque sodium 50% should always be injected at body temperature.

General and Specific Adverse Reactions: Adverse reactions, usually of a minor nature, have occurred in 10-14 per cent of patients who have received Hypaque intravenously. Reactions due to *faulty technique* include hematomas and ecchymoses, following extravasation from the vein, and pyrogenic reactions. *Hemodynamic reactions* include vasodilatation with flushing, hypotension and, rarely, vein cramp or thrombophlebitis. Serious *cardiovascular reactions* include rare cases of cardiac arrhythmias (e.g., ventricular fibrillation), shock, and cardiac arrest. Transient proteinuria may occur occasionally following the injection of radiopaques and, rarely, oliguria and anuria have been reported secondary to a hypotensive reaction. *Allergic reactions* include asthmatic attacks, nasal and conjunctival symptoms, cutaneous reactions such as urticaria and, rarely, anaphylactic shock, sometimes with fatal outcome. Severe reactions may also be manifested by signs and symptoms relating to the *respiratory system* (dyspnea, cyanosis, pulmonary or laryngeal edema), or to the *nervous system* (restlessness, confusion, or convulsions). *Other reactions* include nausea, vomiting, excessive salivation, anxiety, headache, and dizziness. Infrequently, "iodism" (salivary gland swelling) from organic compounds appears two days after exposure and subsides by the sixth day. Reactions to drip infusion pyelography may not appear until some hours after the examination.

Angiography (Peripheral Arteriography and Venography)

Precautions *(See also General Precautions):* Extreme caution is advised in considering peripheral arteriography in patients suspected of having thromboangiitis obliterans (Buerger's disease). Any procedure (even needling or insertion of a catheter) may induce a severe arterial and/or venous spasm. Caution is also advisable in patients with severe ischemia associated with ascending infection.

Adverse Reactions *(See also General Adverse Reactions):* In addition to those listed under General Adverse Reactions, are those due to arterial trauma during the procedure (i.e., needling, insertion of catheter, subintimal injection, perforation, etc.) as well as to the hypertonicity or effect of the medium; also reported are transient arterial spasm, extravasation, hemorrhage, hematoma with tamponade, injury to nerves proximal to artery, thrombosis (rare in venography; if vein is irrigated following injection), dissecting aneurysm, arteriovenous fistula, (e.g., with accidental perforation of femoral artery and vein during needling) transient leg pain from contraction of calf muscles in femoral arteriography; transient hypotension after intraarterial (brachial) injection, and brachial plexus injury with axillary artery injections.

Cerebral Angiography: Because of the special techniques required, it is recommended that Hypaque sodium be used for this purpose only by persons skilled and experienced in carrying out this procedure.

Contraindication: Carotid angiography should be avoided during the progressive period of a stroke, since this increases the risk of cerebral complications.

Precautions *(See also General Precautions):* Select patients for this procedure with care. Use the 50 per cent solution with caution in extreme senility (but not old age, *per se*); advanced arteriosclerosis; severe hypertension; and cardiac decompensation.

The diagnostic value of the procedure, according to many authorities, when employed early enough in locating lesions amenable to surgery, may outweigh the added risk to patients who have recently experienced cerebral embolism or thrombosis (stroke syndrome). A small number of postangiographic fatalities, including progressive thrombosis, have occurred in which the procedure did not appear to play a role. Patients with severe cerebrovascular disease may be examined primarily by indirect methods of angiography.

Care should be exercised to avoid contaminating catheters, syringes, needles, and contrast media with glove powder or cotton fibers.

Angiography is hazardous in subarachnoid hemorrhage. In migraine, the procedure can be hazardous because of ischemic complications, particularly if performed during or soon after an attack.

Adverse Reactions *(See also General Adverse Reactions):* The major sources of complications are faulty technique, occlusive atherosclerotic vascular disease, repeated injections of the contrast media, and higher doses than those recommended.

Untoward reactions are mostly mild and transient, although permanent visual field defects and deaths have been reported.

(continued on next page)

(continued from preceding page)

Hypaque® 50%
sodium
brand of **sodium diatrizoate**

Sterile Aqueous Injection
(Weight/Volume)

Vascular reactions: flushing, vessel spasm, thrombophlebitis, and cutaneous petechiae.

Neurologic complications: transient cerebral blindness, neuromuscular disorders, convulsions, coma, hemiparesis, unilateral dysesthesias, visual field defects, aphasia, and respiratory difficulties.

Aortography

Precautions *(See also General Precautions):* Special caution is advised to avoid inadvertent intrathecal injection when using the translumbar technique. The incidence and severity of reactions or complications that may occur are influenced by: the care and experience with which the procedure is performed; the amount and type of medium used; the age and condition of the patient; and the premedication and anesthesia used. Since aortography is not without some danger, it should be performed only by those experienced in the technique. Wherever possible, repeated injections of the solution during a single study should be avoided.

Adverse Reactions *(See also General Adverse Reactions):* Renal damage and shutdown; neurologic complications such as transverse myelitis or paraplegia; cardiovascular complications such as shock, cardiac arrest or failure, coronary occlusion, arterial thrombosis, embolism, and perforation of vessels; extravasation or hemorrhage from the puncture site or retroperitoneal catheter perforation; necrosis of the intestinal wall; acute pancreatitis; deaths; diffuse cutaneous petechiae; subintimal injection and aortic dissection.

Intraosseous Venography

See General Precautions and Adverse Reactions. A general anesthetic is sometimes necessary since the method is painful. Occasionally, extravasation of the contrast medium from the needle into the soft tissue may occur.

Direct Cholangiography

Precaution *(See also General Precautions):* This procedure should be used with caution in the presence of acute pancreatitis, injecting no more than 5 to 10 ml. without undue pressure.

Adverse Reactions *(See also General Adverse Reactions):* These may be attributed to injection pressure or excessive volume of the medium, resulting in overdistention. Such pressure may produce a sensation of epigastric fullness, followed by moderate pain in the back or right upper abdominal quadrant, which will subside when injection is stopped.

Some of the medium may enter the pancreatic duct and cause a transient serum amylase elevation 6 to 18 hours later, without apparent ill effects. Pancholangitis resulting in liver abscess has been reported. Occasionally, nausea, vomiting, fever, and tachycardia have been observed.

Hysterosalpingography

Contraindications: Menstruation, active or imminent; infection in any part of the genital tract, including the external genitalia; pregnancy, known or suspected. Use not advised for six months after end of pregnancy, or 30 days after conization or curettement.

Precaution *(See also General Precautions):* Caution should be exercised in patients with known or suspected carcinoma to avoid possible spread of the lesion by the procedure.

Splenoportography

Precautions *(See also General Precautions):* Procedure should be performed with caution on patients with blood dyscrasias, a tendency to severe bleeding, or a spleen recently become tender and palpable.

Adverse Reactions *(See also General Adverse Reactions):* Persistent hemorrhage with hemoperitoneum has been reported, and, in some instances, hemorrhage has required splenectomy.

How Supplied: Ampuls of 30 ml., boxes of 1, 10, and 25. A 1 ml. sensitivity test ampul is furnished with each ampul. Vials of 20 and 30 ml., rubber stoppered, boxes of 1, 10, and 25. Vials of 50 ml., rubber stoppered, boxes of 1 and 10. Each vial contains sufficient excess to permit withdrawal of 1 ml. for testing sensitivity.

If the solution is chilled, crystals may form but will readily dissolve if the ampul or vial is placed in moderately hot water before use. Cool to body temperature before injecting.

Winthrop

WINTHROP LABORATORIES, New York, New York 10016

PIONEERS IN PRODUCTS FOR RADIOLOGIC DIAGNOSIS

Bright-image fluoroscopy on wheels.

Picker's "Surveyor" lets you wheel the best in fluoroscopy to any needed location. At the bedside, in the emergency or operating room, in the coronary care suite... wherever you find a standard 110 V, 20 amp. outlet... you can have the advantages of modern image-intensified fluoroscopy.

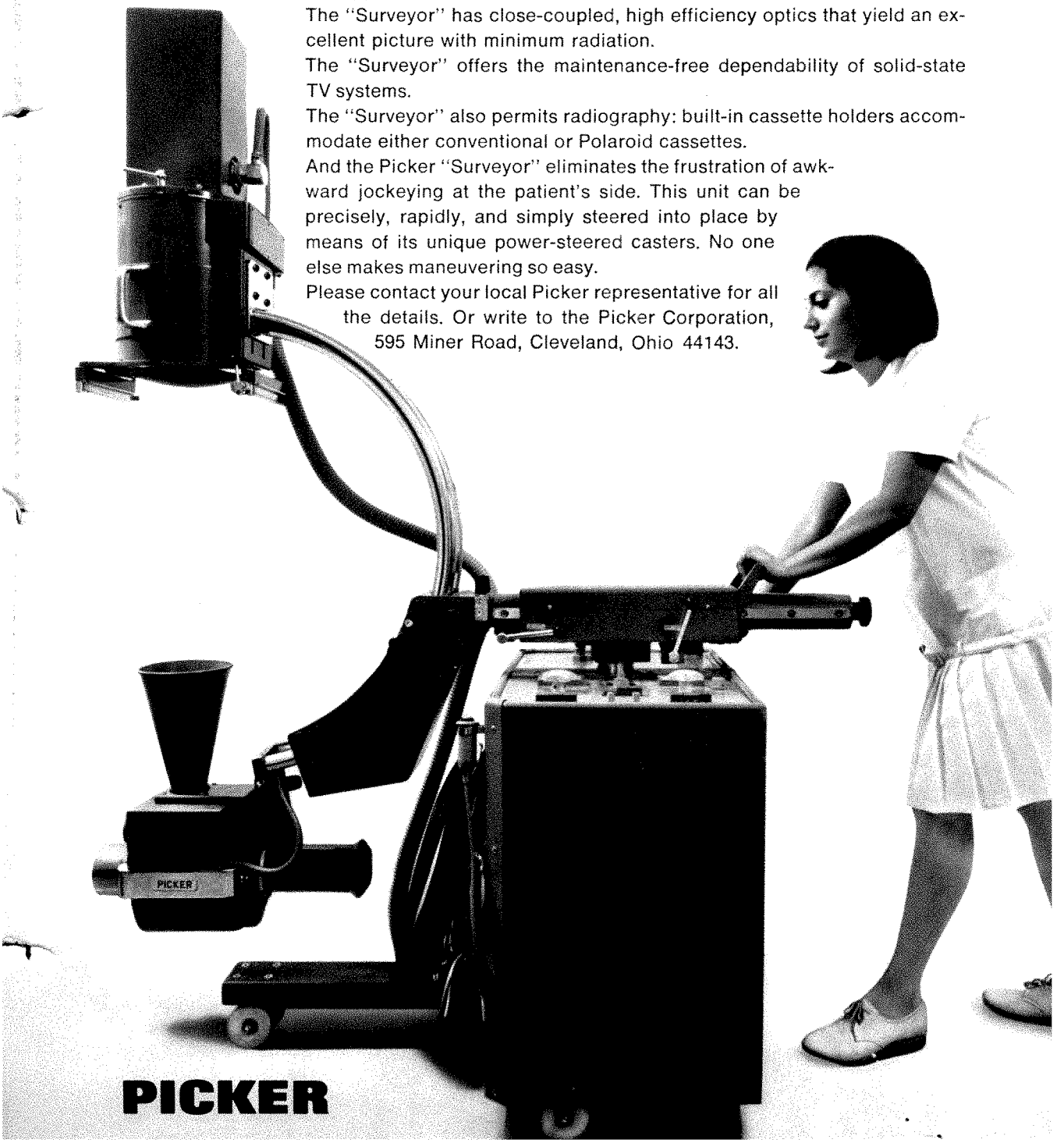
The "Surveyor" has close-coupled, high efficiency optics that yield an excellent picture with minimum radiation.

The "Surveyor" offers the maintenance-free dependability of solid-state TV systems.

The "Surveyor" also permits radiography: built-in cassette holders accommodate either conventional or Polaroid cassettes.

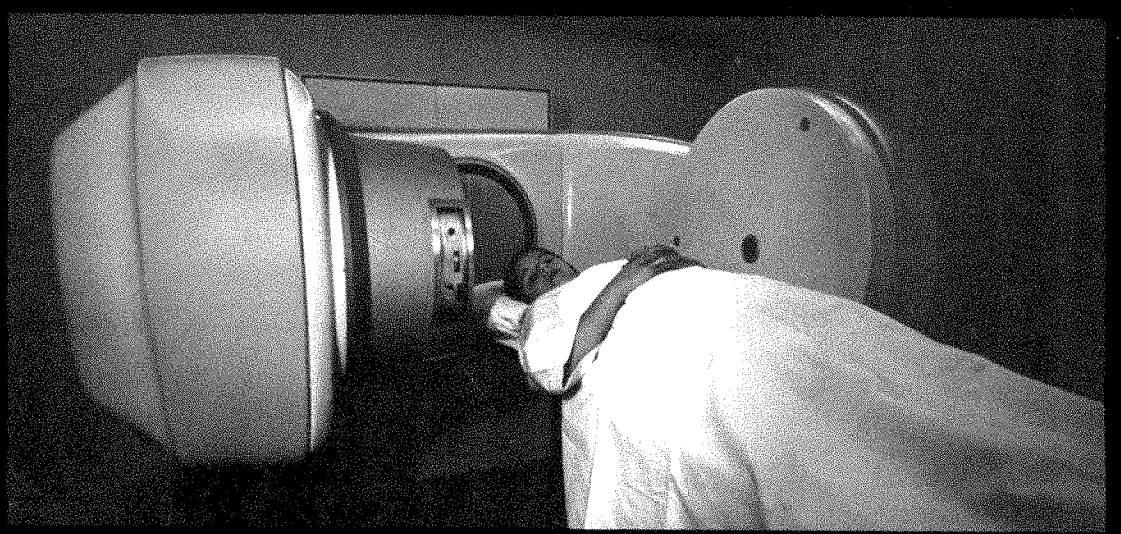
And the Picker "Surveyor" eliminates the frustration of awkward jockeying at the patient's side. This unit can be precisely, rapidly, and simply steered into place by means of its unique power-steered casters. No one else makes maneuvering so easy.

Please contact your local Picker representative for all the details. Or write to the Picker Corporation, 595 Miner Road, Cleveland, Ohio 44143.

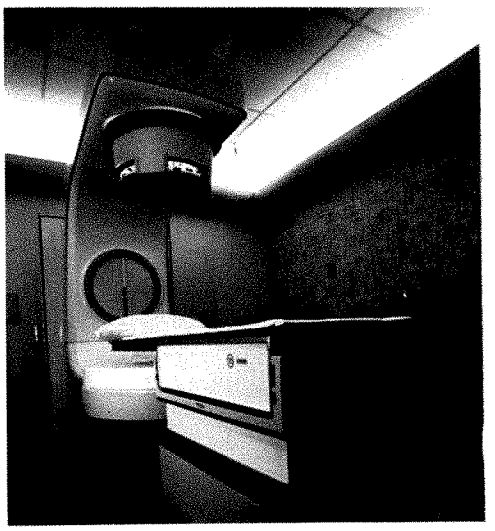


PICKER

The most advanced radiotherapy equipment isn't developmental. It's working now.



Clinac 4, now working at O'Connor Hospital, San Jose, California, USA.



Varian's Clinac® 4, a linear accelerator for deep radiotherapy, is now installed and working at its daily treatment task. Clinac 4 is now said by many to be the most advanced radiotherapy tool available. There's a reason.

Clinac 4 is the result of more than one-half million dollars in direct development costs by one of the nation's leaders in scientific instruments. Clinac 4 is the end product of ten years of medical accelerator experience and nearly two years of continuous factory testing.

Unprecedented large fields and uniform high intensity allow even the "mantle" treatment to be completed with ease in 2 to 3 minutes. Briefly, the advantages of Clinac 4 are high output —up to 350 Rads/min in field sizes up to 32x32 cm—minimum penumbra because of the very small spot size, reliability, and simplified controls to provide ease of use and savings in setup and treatment time. Through engineering excellence, single, multiport and rotational therapy are simplified.

Operational simplicity, reliability, knowledgeable engineering— Clinac 4. For full information, contact Varian Radiation Division, 611 Hansen Way,
Palo Alto, California 94303;
Springfield, New Jersey 07081;
Varian A. G., Zug, Switzerland.

varian
radiation division

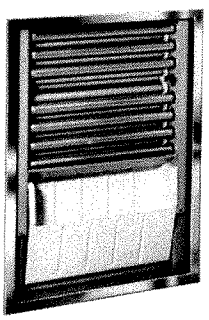


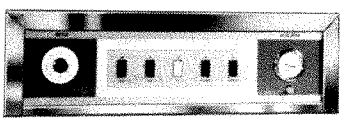
NEW
Pakorol-XU... the

newest processor for x-ray film... already more than a year old. (*That's how long it has been tested in hospitals, clinics and offices.*) In just a little over 5 square feet of light area, it produces unequalled quality results... in as little as 90 seconds. The Pakorol-XU can be adapted to other standard processes, too.



The new transport system uses paired rollers—one hard, one soft. Their squeegee action eliminates film streaking. The dryer dries films thoroughly at low temperature—a must for quality RP film. It eliminates heat marking. For the operator's convenience, controls are on an eye-level panel. And to really simplify maintenance, all plumbing and electrical components are easily accessible by removing one panel below the feed table.





There's much more. If you (or your department) process radiographs, you must see the new Pakorol-XU. Ask your Pako Distributor or send the coupon for more information.

PAKO CORPORATION PAKO
6300 Olson Memorial Highway, Minneapolis, Minnesota 55440

PS Processing Systems for the Photographic, Graphic Arts, Motion Picture, Medical and Industrial X-Ray Industries.

PAKO CORPORATION
6300 Olson Memorial Hwy. • Minneapolis, Minn. 55440

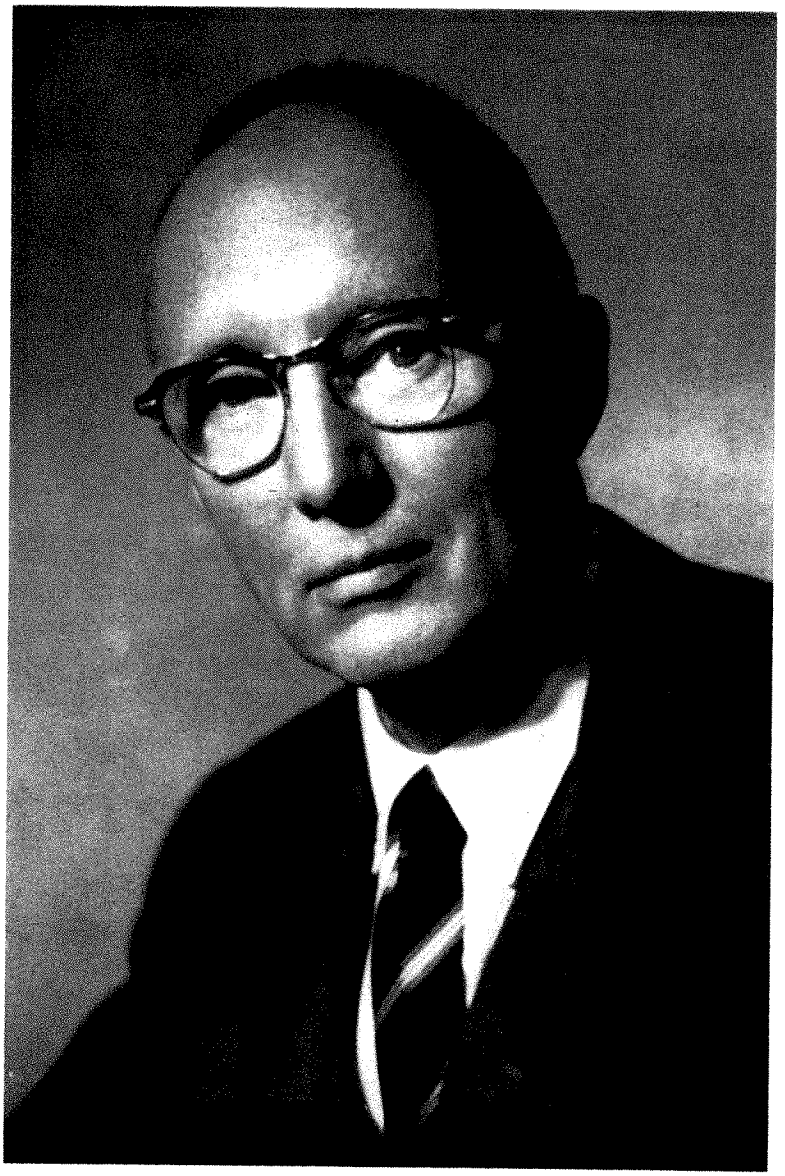
Please rush me complete information on the New Pakorol-XU

Hosp/Clinic/Office .....

ADDRESS .....

CITY ..... STATE ..... ZIP .....

NAME .....



JOHN L. POOL, M.D.

THE AMERICAN JOURNAL OF ROENTGENOLOGY
RADIUM THERAPY AND NUCLEAR MEDICINE

VOL. 105 JANUARY, 1969 NO. 1

THE ROLE OF THE SPECIALIST IN MEDICINE AND SOCIETY*

THE PRESIDENT'S ADDRESS, 1968

By JOHN L. POOL, M.D.
NEW YORK, NEW YORK

IN WELCOMING members and guests to this Fiftieth Annual Meeting of our American Radium Society, the honor of introducing the subject matter and theme of this meeting is one that I truly cherish and also feel to be a great burden. Particularly so, as I recall the messages brought to us in recent years by successive friends and colleagues who have had this same opportunity, and in earlier years the inspiring words of wisdom and guidance that teachers and preceptors in the role of president have set before us. The purposes and justifications for the activities of the American Radium Society—and for other specialty groups—are worthy of review and consideration from time to time.

This year seems to me, once again, an appropriate moment to remember where we have been in the previous 49 meetings and to consciously try and direct where we might justifiably, usefully, and most fruitfully go in years ahead. As witnessed by the enthusiasm of our membership in coming to Miami Beach for these Scientific Sessions—and, perhaps, a bit of sun and companionship—and the fact that your Program Committee could hardly use half the offerings for the meeting, there is no question of the good health of our organization. The long list of applicants for membership attests to future vigor. The attention the AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY, AND NUCLEAR MEDICINE commands in the scientific community reflects, in considerable part, the scientific achievements and intellectual capacity of our membership. None of these facts are debatable, but it seems to me worthwhile to consider whether we are now just allowing ourselves to grow along with the times, and whether or not there are areas where more ordered leadership in matters medical should properly fall into our hands.

This Society is certainly a meeting ground for multiple disciplines, and in this day of superspecialization, it is at times hard to know which disciplines to include

* Presented at the Fiftieth Annual Meeting of the American Radium Society, Miami Beach, Florida, April 7–11, 1968.

and which to exclude. There never has been exclusion of applicants who fulfill the objective of the Society so clearly stated in the constitution, *viz*, " . . . to promote the scientific study of radium and other sources of ionizing radiation in relation to their physical properties, their biological effects and their therapeutic application and to encourage liaison between the various specialties concerned with the treatment of cancer." Nevertheless, over the years there has been some pendulum swing in the content of programs towards and away from special interests within the Society. A quarter century ago, a strong effort to emphasize all aspects of cancer care in our deliberations did not meet with membership support and the trend towards radiotherapeutic matters became so strong that 9 or 10 years ago one program contained not a single paper of predominantly surgical content. Such variations in format for meetings should express the interests of many members and not just the principal interests of a momentary leadership.

Historically, medical knowledge is changing. It is difficult for one man now-a-days to be proficient in many separate disciplines. We can look back with great admiration on a scientist such as Marie Curie. Her birth centenary was noted, I am sure, by us all last November, and at the time our Society was founded she was able to encompass in one mind the frontiers of knowledge in physics and chemistry, and the applications of radioactive materials to biologic sciences and in medicine. Or, take the case of that versatile physician, Henry Janeway, honored in our Society. He was a dermatologist practicing in New Brunswick, New Jersey, in the period 1905–8, and undertook the use of radioactive materials in his specialty, later expanding their use to body cavities and tumor implants. In desiring to improve the treatment of the cancer patient, he studied pathology and so, became acquainted with James Ewing who brought him to Memorial Hospital in 1913 as an expert in radiation therapy and surgery. Furthermore, Dr. Janeway was a student and investigator of pulmonary physiology. He worked at the Rockefeller Institute with H. W. Meyer on the negative pressure chamber and with Meltzer on insufflation anesthesia, or positive pressure anesthesia, and was a founder of the American Association for Thoracic Surgery. Thus, here were combined in one individual abilities of several disciplines and his bibliography reflects contributions in anesthesia, physiology, pathology, surgery, dermatology, and predominantly, the uses of radiation therapy. What single man can encompass so much medical knowledge today? Or, is it wise for an individual to attempt to be proficient in so many fields?

Our hospitals make efforts to integrate the treatment of an individual patient by varied specialists through the encouragement of consultation and the establishment of combined clinics. But, by and large, hospital practice also confines a man's daily work to a narrow field. Over the years the hardening of people in specific areas of specialization has been encouraged by the multiplication of specialty boards of which there are now 24. One clear duty of national societies is to bring all of us out of our corners and encourage viewing of the whole broad picture of illness, and to learn what others know which reflects directly on our own work.

"The mind of man works with strangeness upon the body of time" wrote Virginia Woolf in Orlando, and the specialist physician needs to spend his time for the general weal as well as for the individual woe.

The problem of specialized teaching in medical schools is one well-known to all faculty members. There is such vying for the student's mind and time from the dean's office, that sometimes it almost seems as though the patient for whose benefit all the learning is destined is lost in the shuffle. There are many approaches to the attempt to indoctrinate the embryo physician in all specialty areas. These have included courses which are oriented entirely to the laboratory; other courses which are oriented entirely to the office

patient including his social and economic environment; and courses oriented towards organ systems, which bring laboratory and clinical aspects of say kidney diseases to the student at the same time.

Can we in the Societies learn from the ever-changing efforts of the medical schools to improve teaching techniques? After all, the major function of a Society such as ours is the teaching one; the mutual exchange of new ideas is why we are here. Presentation of our cherished notions dressed up with what we hope are objective facts and figures are presented here with the expectation that our colleagues from across the land will be receptive. And, who knows, may even emulate what we recommend. Ready acceptance is the public atmosphere of most National Meetings and friendship, fear of offence, and lack of strong convictions may, at times, prevent the voicing of dissent and the presentation of contrary evidence in open meetings. It will be all too evident every afternoon and evening this week—at the pool side—along the golf course—in the many rooms of this hotel—that dissent is present, disagreement does exist and differences of opinion are part and parcel of the medical educational process.

Are we right to be silent in the open forum when statements are made with which from our own experiences we disagree? Or, when facts are presented the interpretation of which would be altered by the presentation of facts within our ken. There is indeed a fine line between opinionated disagreement and objective or constructive re-coloring of part of a picture painted, or re-orientation of portions of an idea expressed or conclusion drawn. Is it not in the best interest of furthering the ideals of our Society for us all to prepare ourselves in the areas of our special knowledge and to challenge in the open forum conclusions and facts with which we have substantial reason to disagree? Perhaps, here lies an area in Postgraduate Medical Education where a Society such as ours can lead. Let us not lose sight of the experimental method in our techniques of presentation. We have been hypnotized for many years into conforming to the use of lantern slides and plain films. Once indeed hypnotism of a member was demonstrated before us all, and perhaps we need consider better and more frequent use of the modalities of the communications industry, such as closed circuit television, accelerated speech mechanics, and other electronic aids. Last year Drs. Friedman and George introduced the principle of television tape recording of meeting personalities and highlights. This program will be continued to enlarge the audience available for our discussions.

The proliferation of Journals and especially Societies is certainly an exciting and, usually, heartwarming evidence of medical thirst for new knowledge. It seems right and just that there should be a place in the sun for everyone who wants to speak out. Older Societies such as ours seem duty-bound—to me anyhow—to offer special educational opportunities not obtainable in any other way. Frank and open discussion is one such extra value we can provide.

Another value is our happy opportunity to bring together representatives of so many disciplines in medicine—men who work in so many different aspects of the cancer problem. The future membership of this Society is dependent on actions of the current membership and the type of man who will be at the 55th meeting is the responsibility of you and me here today at the 50th. Our membership is not homogeneous. Heaven forbid that we be all of a piece. But I think that we should take a fresh look at our membership roster and ask ourselves whether our programs and friendships are such as to attract cancer workers in the fields of isotopes, leukemia, brain tumor, childhood cancer, surgery and all its subspecialties, as well as the radiation therapist who now predominates. Without enumerating quotas, our forums can be improved by encouraging men in all fields of cancer therapy to offer themselves for membership in the American Radium So-

ciety. As Ralph Waldo Emerson put it: We are of different opinions at different hours but we may be said to be at heart always on the side of truth.

Our relationships with other Societies seem appropriately competitive and yet friendly. It is not too soon for all of us to be looking forward to the year 1972, when a Joint Meeting with the James Ewing Society and The Society of Head and Neck Surgeons will take place. Such Joint Meetings with other bodies and different ones at that can be encouraged. They should allow some years, perhaps a different format, where a single problem is analyzed and discussed from as many specialty points of view as exist. Some such subjects include: preoperative radiation therapy; methods of preventing cancer dissemination during surgery and irradiation; the improvement of diagnostic skills by combinations of radiographic and endoscopic techniques.

Finally, we must face the fact that physicians and their Societies do not exist separate from the communities in which we live. Are we in our Radium Society only serving our own interests? Or, are there some ways that we can better serve the medical community as a whole? Certainly I would not be one to suggest despite these troubled soul-searching times that this Society of ours should have political overtones, or deliver political messages. We have appropriate medical organizations in that field. However, Dr. Howard Taylor said: become in some degree a part of government, attempt to guide its progress, and so preserve some of what seems essential to the traditional ideals of medicine.

We have always welcomed non-members to our Meetings and have, I trust, made them feel at home. Maybe we should do more in such encouragement. One area that might be considered has to do with training programs. The Society could usefully consider supporting a fellowship for training—the training to be for properly qualified young men or women from other lands and under the personal guidance of some of our members. Prizes to encourage investigative work by trainees is another mechanism that we could employ to encourage the ideal, original investigation in our field of interest. The past 50 meetings have been occasions of intellectual stimulus, warm and continuing friendship, and advancement and dissemination of new information for three generations of physicians. May we continue as well in the future.

T. S. Eliot said, "We shall not cease from exploration and the end of all our exploring will be to arrive where we started, and know the place for the first time."

755 Park Avenue
New York, New York 10021

VOL. 105, NO. 1

ESTHESIONEUROBLASTOMAS*

A REPORT OF 7 CASES

By LEONIDAS CASTRO, M.D.,†‡ SAMUEL DE LA PAVA, M.D.,§ *and* JOHN H. WEBSTER, M.D.‡
BUFFALO, NEW YORK

THE olfactory neuroblastoma or esthesioneuroblastoma is a malignant neoplasm arising from the olfactory mucous membrane. The occurrence of this type of tumor is uncommon and most of the reports have been scattered throughout the European literature, especially the French literature.

Berger, Luc and Richard[3] in 1924 described the first case, followed 2 years later by another case of intranasal neurogenic tumor described by Berger and Coutard.[4] In 1951, Schall and Lineback[9] collected 14 cases from the literature and added 3 cases of their own. In the same year, Seaman[10] reported another case. Becker and Jacox[1] in 1964 made a survey from the literature and found 63 cases which, when added to the 5 cases in their report, brought the total to 68 cases. In February 1965, Fitz-Hugh and his collaborators[5] reported 6 cases, and in the same month, Lewis *et al.*[7] published a report of 18 cases which had been followed for 5 to 27 years at the Memorial Center for Cancer and Allied Diseases. In July of 1965, Gerard-Marchant and Micheau[6] reported an additional 5 cases from the Institut Gustave-Roussy.

The purpose of this paper is to present an additional 7 cases which have been seen and treated at Roswell Park Memorial Institute since 1960. A diligent search in our records and histologic files has failed to reveal a single case treated at this Institute prior to that date.

PATHOLOGY

Although the histology of this type of intranasal tumor often presents difficulty for the pathologist, the following criteria are generally accepted.

These tumors are composed, in general, of round, oval or even slightly fusiform cells that may form rosettes; however, they did not do so in our cases. In the absence of rosettes, the presence of neurofibrils would be helpful in making a diagnosis. The cells are ordinarily the size of a lymphocyte or slightly larger. The cytoplasm is usually poorly defined and although there is nothing absolutely characteristic in the cells, the trained observer finds them different from either lymphocytes or reticular cells (Fig. 1). One feature that is of more help, when present, is a certain compartmentation of the neoplasm resembling lobulation and is due to fibrosepta in the tumor. These are described by Obert *et al.*[8] and are best seen under low magnification (Fig. 2).

Although our experience is certainly limited, we find ourselves in agreement with Becker and Jacox[1] that it does not seem necessary to divide this neoplasm into esthesioneuroepitheliomas (with rosettes), esthesioneuroblastomas (with pseudorosettes) and esthesioneurocytomas with neither rosettes nor pseudorosettes, since these features are most likely different aspects of the differentiation of the same tumor, and at this stage it would not be safe to correlate differentiation with prognosis. An excellent discussion of the difficulties encountered in diagnosing this tumor can be found in the recent paper by Gerard-Marchant and Micheau.[6]

REPORT OF CASES

CASE 1. This 48 year old white male was first seen in this Institute in December, 1959 with a 3 year history of nasal obstruction and bleeding from the right side of the nose. Two months before admission, a surgical removal of a large

* Presented at the Sixty-eighth Annual Meeting of the American Roentgen Ray Society, Washington, D. C., September 26–29, 1967.
From the Departments of Therapeutic Radiology‡ and Pathology,§ Roswell Park Memorial Institute, Buffalo, New York.
† Present Address: Director of Radiotherapy Department, Ohio Valley General Hospital, Wheeling, West Virginia.

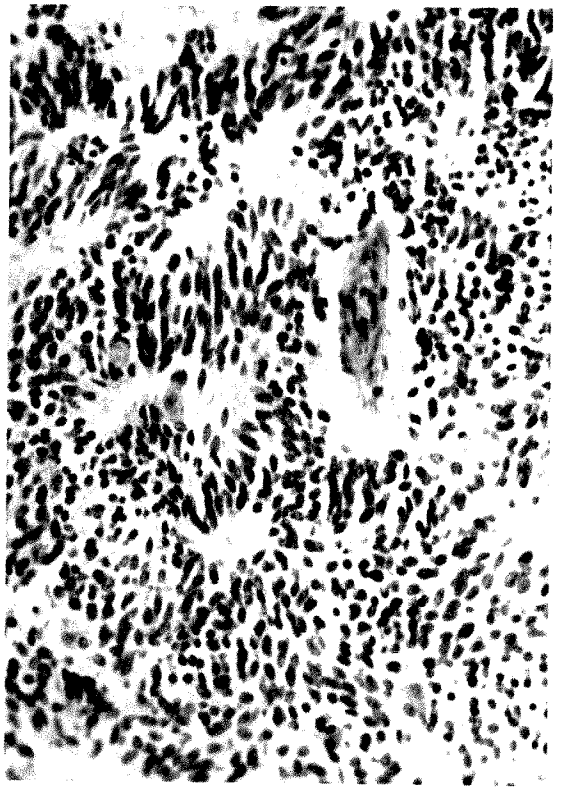


FIG. 1. Photomicrograph (×400) of a typical section of esthesioneuroblastoma showing the poorly defined cytoplasm and some attempt at rosette formation.

intranasal tumor occupying the right nasal cavity with protrusion into the nasopharynx was undertaken. This had been followed by cobalt 60 teletherapy for a tumor dose of 6,000 r in 43 days. Review of the microscopic slides at this Institute revealed esthesioneuroblastoma. The patient shortly developed a recurrence on the right posterior nasopharyngeal wall which was proved by biopsy. This was treated by intracavitary radium to a dose of 6,000 gamma r at 2 cm. depth over 12 days (June 6, 1960 to June 17, 1960). The patient has been followed regularly up to the present and is free of disease. As a sequel he has a fibrotic and somewhat functionally defective soft palate.

CASE II. This 60 year old white male developed spontaneous epistaxis in October, 1960. Following repeated recurrence of the bleeding, the patient was hospitalized. Nasal polyps were noted on physical examination and a polipectomy was performed in December, 1960. Histologic examination revealed neuroblastoma. The patient was then referred to Roswell Park Memorial Institute and on review of the microscopic slides, esthesioneuroblastoma was identified.

On February 23, 1961 the left paranasal sinus region was explored and removal of the tumor from the ethmoid, frontal and the maxillary sinuses was carried out together with removal of the cribriform plate and partial resection of the dura. Sections of the specimen confirmed the pathologic diagnosis of esthesioneuroblastoma, but revealed that the lesion was not completely excised. Following the healing of the surgical wound, the patient was treated with radium utilizing two parallel tandems loaded with 70 mg. of radium, 1 mm. Pt filtration, which were inserted in the nasal cavity for a mucosal dose of 7,000 gamma r fractionated over 13 days. The patient remained free of disease until May, 1963 when a small recurrence was discovered at the left ethmoid sinus. On May 26, 1963 a resection of the nasal septum and exploration of the right

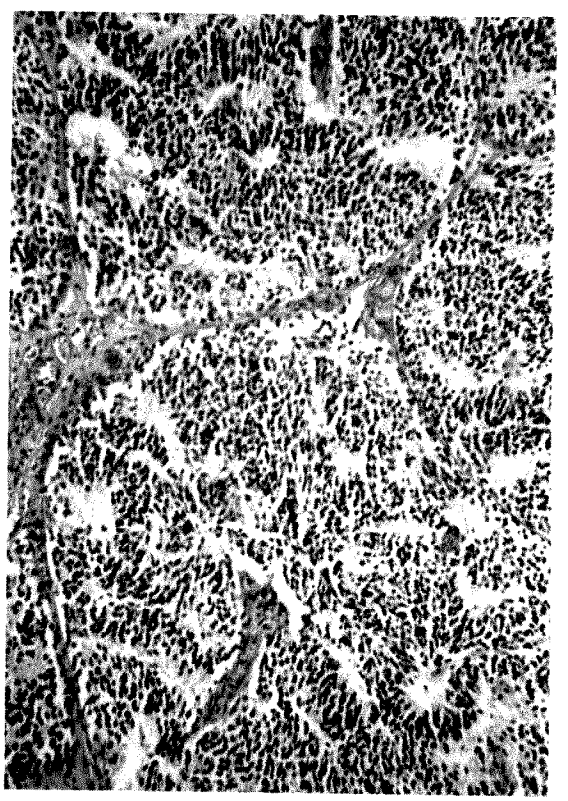


FIG. 2. Another section (×200) showing the fibrosepta which are helpful in making the diagnosis.

ethmoidal region was carried out with removal of the recurrent tumor. The patient unfortunately developed cerebral edema with further postsurgical complications and died on August 19, 1963. The autopsy revealed no residual tumor. (Today, this patient would have been treated with a teletherapy source to achieve uniform irradiation of the entire volume which had borne tumor at any time, since accurate radium placement at the site of this recurrence is very difficult.)

Case III. This 41 year old white female was first seen in our Institute on May 3, 1962 with a 5 year history of epistaxis. A polyp had been removed in 1956, followed by "radiation therapy" for recurrent epistaxis. Just prior to her admission to the Institute a tumor had been found in the right ethmoid region and right nasal passage. At biopsy esthesioneuroblastoma was reported.

Physical examination revealed multiple polypoid lesions in the right nasal fossa with bulging into the right nasopharynx. The patient also had poor vision in the right eye attributed to orbital involvement. Roentgenography of the maxillary sinuses showed cloudiness of both maxillary antra, the presence of a soft tissue mass in the right nostril, bony destruction of the medial wall of the right maxillary antrum and a protrusion of the mass into the antrum itself. On May 28, 1962 a right lateral rhinotomy with exploration and curettage of the ethmoid sinus, maxilla, sphenoid ridge and orbital region was performed. The sphenoid ridge and nasal cartilage were destroyed and the ethmoid sinuses were involved.

Surgery was followed by roentgen therapy to the right anterior and lateral face using wedge filter fields to a tumor dose of 6,265 rads in 45 days (2 mvp., half-value layer of 7.6 mm. Pb, source-skin distance of 100 cm.).

The patient seemed free of disease until April, 1964 when she developed symptoms of spinal cord compression at the level of D3-D5 (Fig. 3). Laminectomy revealed an intramedullary spinal cord metastasis,[2] and she was treated with irradiation using the above 2 mvp. factors to a tumor dose of 5,000 rads in 45 days. She obtained good symptomatic response.

A few months later she developed complete paralysis of the lower extremities and a laminectomy at D10-L1 was performed. Tumor was again found, this time growing diffusely through the subarachnoid space. Radiation therapy to that area was given through a single posterior field to a tumor dose of 3,000 rads in 4 weeks using the above 2 mvp. factors. The patient continued to deteriorate with further progression of her neurologic symptoms as well as recurrence at the primary site with exophthalmos and ptosis of the right eye, and in spite of palliative measures died from her disease on December 19, 1965. Autopsy revealed extensive widespread metastatic esthesioneuroblastoma.

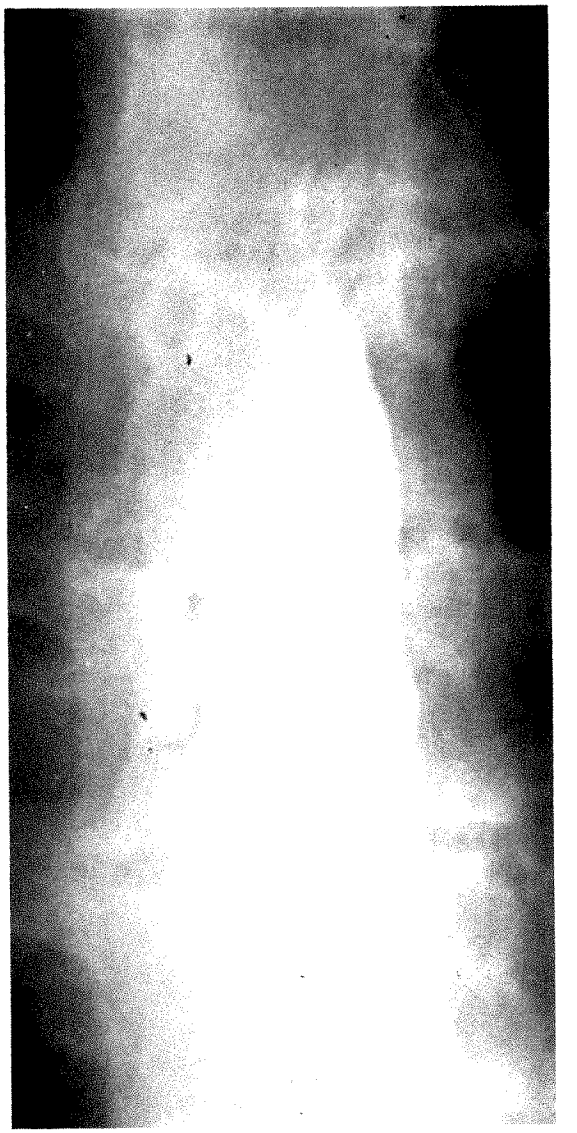


Fig. 3. Case III. Myelogram taken in April, 1964 just prior to laminectomy at which an intramedullary spinal cord metastasis was found in the region of D3 to D5.

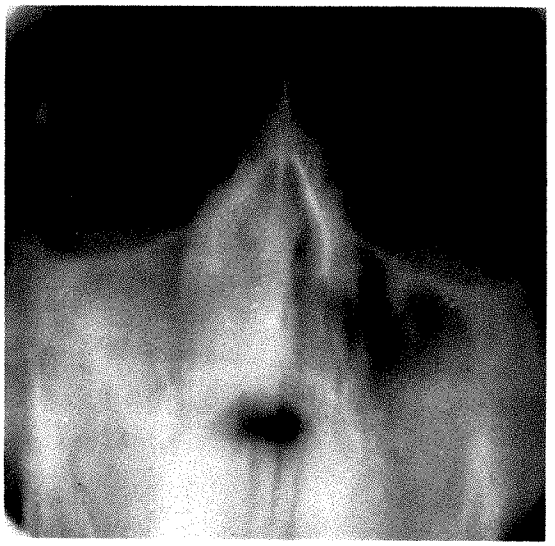


FIG. 4. Case IV. Roentgenogram of the affected area showing cloudiness of the right antrum, a soft tissue mass in the right nasal cavity and destructive changes in the medial wall of the right maxillary antrum and in the floor of the right orbit, posteriorly.

CASE IV. This 67 year old white female was first seen in our Institute on December 6, 1962 with a history of right nasal obstruction and bleeding of 8 months' duration. A large intranasal mass was seen on physical examination and a biopsy taken showed esthesioneuroblastoma. Roentgenography and laminagraphy of the paranasal sinuses showed a soft tissue mass in the area of the right nasal cavity with clouding of the right maxillary antrum, and destructive changes in the medial wall of the right maxillary antrum and floor of the right orbit posteriorly (Fig. 4). On December 14, 1962 a right maxillary antrectomy was performed (Fig. 5) followed by radiation therapy through 2 converging lateral and 1 anterior facial fields using the 2 mvp. generator, half-value layer of 7.6 mm. Pb. A tumor dose of 5,200 rads was delivered in 35 days. The patient was followed regularly until her death from bronchopneumonia on November 28, 1966. At no time was there evidence of recurrent or metastatic disease.

CASE V. This 16 year old white male patient was seen on March 26, 1963 with a history of right nasal obstruction and swelling of the nose. Two weeks prior to admission, a right nasal tumor was removed. Review of the pathologic sections in this Institute revealed esthesioneuroblastoma. On examination, remnants of the tumor mass were found involving the upper turbinate and ethmoid areas (Fig. 6). No pal-



FIG. 5. Case IV. Roentgenogram illustrating the extent of the resection undertaken just prior to definitive radiation therapy.

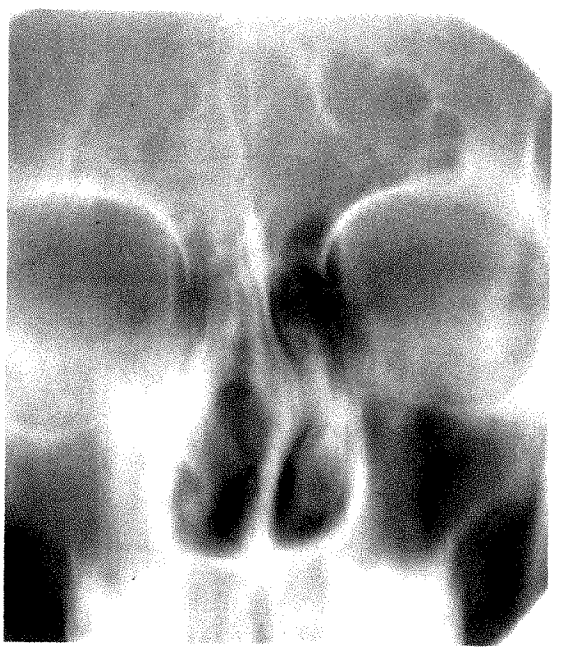


FIG. 6. Case V. Roentgenogram showing tumor involvement in the region of the upper turbinate and ethmoid sinus prior to surgery.

pable cervical lymph nodes were present and no other metastases were found. The nasopharynx was clear.

On April 1, 1963 a right rhinotomy, turbinectomy, antrotomy and excision of the tumor was done (Fig. 7). This excision was followed by radiation therapy using a 2 mvp. generator, half-value layer of 7.6 mm. Pb through 1 anterior field of 5×7 cm. Between April 10, 1963 and May 9, 1963 a tumor dose of 4,600 rads was delivered. The patient has been examined regularly to the present time and he is free of disease.

Case VI. This 42 year old male was seen on May 5, 1964 with a history of frontal headaches of 2 months' duration and swelling of the right neck, as well as bulging of the right eye. The patient was confused and hallucinated and no further history was available. The physical examination disclosed marked weight loss, exophthalmos of the right eye with a large hard mass of the lymph nodes in the right midcervical area and a recent scar in the right supraclavicular area from a biopsy, which was reported as undifferentiated carcinoma in a cervical lymph node following carcinoma of an unknown origin. Chest roentgenography, intravenous pyelography and skeletal survey were reported as negative. His condition deteriorated very rapidly and he expired on May 30, 1964. The autopsy revealed extension from a tumor involving the orbit with metastases to the right cervical, mediastinal, axillary and retroperitoneal lymph nodes, vertebrae and ribs, liver, lungs, and adrenal and pituitary glands. The histologic diagnosis was esthesioneuroblastoma.

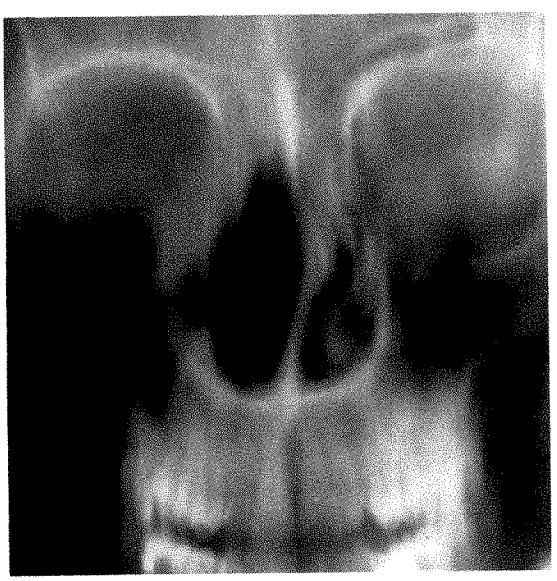


Fig. 7. Case v. Roentgenogram following surgery showing the extent of the surgical defect.

Case VII. This 10 year old white male was first seen in the Institute on December 7, 1966 with a history of having had difficulty breathing through his nose for about 4 weeks. He had been unsuccessfully treated with antibiotics since the onset of this symptom. Immediately prior to admission, he had been seen by an ear, nose and throat consultant who discovered a nasopharyngeal tumor. His past history was entirely noncontributory.

Physical examination revealed a well-developed, well-nourished apparently healthy boy with noisy respiration and entirely normal physical findings except for the presence of a round, avascular mass in the nasopharynx. The clinical diagnosis of juvenile nasopharyngeal fibroma was made.

On December 9, 1966 the patient was taken to surgery where a 2.5 cm. diameter broad-based tumor of the nasopharynx was excised. A frozen section suggested reticulum cell sarcoma; permanent sections revealed esthesioneuroblastoma.

Following his recovery from surgery, radiation therapy was instituted on December 20, 1966 through 2 bilateral parallel opposing fields using the 2 mvp. generator, half-value layer of 7.6 mm. Pb, source-skin distance of 100 cm., and covering the entire nasopharynx. This was continued until January 26, 1967 at which time a minimum tumor dose of 5,000 rads in the midplane had been delivered.

The patient tolerated the therapy very easily and to this date has remained well with no evidence of recurrence or metastasis.

It is, of course, too early to speculate on the eventual outcome in this case; however, it is reported for the sake of completeness and because of the unusual site, the posterior nasopharyngeal wall, and the age of the patient.

TREATMENT

Study of the cases already reported in the literature and our own cases reveals this to be a fairly well-defined clinical entity which usually presents with symptoms of recurrent epistaxis, unilateral nasal obstruction

and sometimes other signs related to local infiltration, such as headaches and unilateral exophthalmos. On examination a polypoid tumor mass is seen most commonly arising from the middle turbinate but not infrequently from the roof of the nasal fossa and in one of our cases, the upper nasopharynx. Metastases to cervical lymph nodes are less common than in carcinoma of the nasopharynx but blood borne metastases to distant sites are, at the least, equally common in late stages of the disease.

As would be expected, the possibility of performing curative surgery in this region is stringently limited by anatomic considerations, and recurrence following local surgery is almost the rule. These lesions, however, tend to be quite radiosensitive, the great majority of cases responding completely to vigorous radiation, at least initially.

While some authors such as Fitz-Hugh *et al.*[5] have recommended the use of preoperative irradiation followed by surgery, most workers have tended to suggest that surgery followed by radiation therapy should be the method of choice.

Patients treated at this Institute, following biopsy and identification of the lesion, have been subjected to exploratory surgery with resection of as much tumor as possible prior to their treatment with irradiation. This method had the advantage of permitting a careful assessment of the extent of the lesion and removal of the great bulk of the tumor prior to the institution of radiation therapy. At a suitable interval following this procedure, a radiation therapy scheme is individually planned to irradiate the entire tumor bearing region as uniformly as possible to a tumor dose of the order of 5,000 to 6,000 rads in 5 to 6 weeks.

Today, supervoltage radiation therapy is uniformly employed because of the greater precision with which it can be administered and because of the almost negligible bone to soft tissue absorption ratio in this region of the energy spectrum. Very occasionally, an intracavitary radium applicator can be fashioned to irradiate the tumor bearing region even more selectively, but this is rarely ideal.

Apparently localized lesions treated in this way appear to have a better than 50 per cent chance of prolonged, if not permanent, local control. It would further appear that relatively small lesions confined to the nasal cavity with little evidence of local extension to neighboring structures are very unlikely to have produced blood borne metastases, but that larger lesions with clear evidence of extension to neighboring structures have a great likelihood of having produced such metastases.

SUMMARY

Esthesioneuroblastoma is a rare tumor of nasal-neurogenic origin which, because of its close resemblance to the neuroblastomas arising in the adrenal region, is difficult to diagnose.

These tumors tend toward local recurrence rather than hematogenous metastases, although the latter occur in advanced cases.

The tumor is quite "curable" and our treatment of choice is excisional surgery followed by local radiation therapy to total tumor doses of 5,000 to 6,000 rads in 5 to 6 weeks.

The literature is reviewed and 7 additional cases are reported in detail, bringing the total to 104 cases in the world literature.

Leonidas Castro, M.D.
Radiotherapy Department
Ohio Valley General Hospital
Wheeling, West Virginia 26003

REFERENCES

1. BECKER, M. H., and JACOX, H. W. Olfactory esthesioneuroepithelioma: experiences in management of rare intranasal malignant neoplasm. *Radiology*, 1964, *82*, 77–83.
2. BELMUSTO, L., OWENS, G., and DE LA PAVA, S. Aspects of intramedullary spinal cord metastases. *New York J. Med.*, 1966, *66*, 2273–2281.
3. BERGER, L., LUC, and RICHARD. L'esthésioneuroépithéliome olfactif. *Bull. Assoc. franç. étude du cancer*, 1924, *13*, 410–420.
4. BERGER, L., and COUTARD, H. L'esthésioneurocytome olfactif. *Bull. Assoc. franç. étude du cancer*, 1926, *15*, 404–414.

5. Fitz-Hugh, G. S., Allen, M. S., Jr., Rucker, T. N., and Sprinkle, P. M. Olfactory neuroblastoma (esthesioneuroepithelioma). *A.M.A. Arch. Otolaryng.*, 1965, *81*, 161–168.
6. Gerard-Marchant, R., and Micheau, C. Microscopical diagnosis of olfactory esthesioneuromas: general review and report of five cases. *J. Nat. Cancer Inst.*, 1965, *35*, 75–82.
7. Lewis, J. S., Hutter, R. V., Tollefsen, H. R., and Fotte, F. W., Jr. Nasal tumors of olfactory origin. *A.M.A. Arch. Otolaryng.*, 1965, *81*, 169–174.
8. Obert, G. J., Devine, K. D., and McDonald, J. R. Olfactory neuroblastoma. *Cancer*, 1960, *13*, 205–215.
9. Schall, L. A., and Lineback, M. Primary intranasal neuroblastoma: report of 3 cases. *Ann. Otol. Rhin. & Laryng.*, 1951, *60*, 221–229.
10. Seaman, W. B. Olfactory esthesioneuro-epitheliomas. *Radiology*, 1951, *57*, 541–546.

INTERSTITIAL RADIATION IN THE MANAGEMENT OF MALIGNANT DISEASE OF THE FACIAL STRUCTURES*

By CARL W. BOYER, JR., LT. COLONEL, MC, USA, THEODORE J. BRICKNER, JR., LT. COLONEL, MC, USA, RONALD H. PERRY, LT. COLONEL, MC, USA, *and* JOHN G. MAIER, COLONEL, MC, USA
WASHINGTON, D.C.

RADIUM implantation is generally performed when it is desired to deliver a large dose of radiation to a small volume of tissue. Considerable experience has been documented using radioactive materials for interstitial implants in the treatment of malignant tumors in many accessible areas of the body. Little information is to be found in the literature, however, describing techniques for implantation of the facial area. Indeed this form of therapy may not even be considered by many radiation therapists. The present report is concerned with an attempt to correct this situation by presenting some cases to illustrate the indications for interstitial irradiation in the facial area and to document the feasibility of the procedure.

REPORT OF CASES

CASE 1. L. S. is a 22 year old man who was found to have a rather extensive fibrosarcoma of the maxillary sinus on the right side. The tumor extended into the nasal cavity through the ethmoidal sinuses and involved the anterior aspect of the sphenoid sinus and floor of the right orbit. Because the tumor was considered to be beyond surgical excision, a course of external radiation therapy was begun. The entire involved volume including the right orbit, was treated through anterior and superior portals using a wedge filter with each portal (2 mvp., half-value layer 7 mm. Pb, target-skin distance 100 cm.). A tumor dose of 6,000 r in 6 weeks was delivered with no remarkable regression of the tumor mass in the maxillary antrum. It was decided to supplement this dose with an interstitial radium implant. Prior to placement of the needles, a Caldwell-Luc procedure was performed with debulking of the residual tumor mass within the maxillary antrum. A double plane of low intensity radium needles was placed in the ethmoidal sinuses, a single plane of 3 radium needles was placed beneath the right eye on the floor of the orbit, and 6 high intensity needles were placed into the soft tissue of the inner aspect of the walls of the maxillary antrum through the surgical defect (Fig. 1, *A* and *B*). In this fashion a tumor dose of 2,000 r was delivered to the residual tumor in 10.5 hours.

For approximately 2 months after the implantation there was considerable morbidity involving the right eye and consisting of photophobia, tearing, and moderate pain. The patient was treated conservatively with eye washes and analgesics. Intermittent temperature elevation and pain in the facial area were attributed to superimposed infection and were treated successfully with antibiotics. The patient left the hospital with relatively few symptoms. He is living and well more than 2 years later with no evidence of active tumor, but is completely blind in the right eye.

Comment. The treatment of this uncommon tumor usually fails to cure the patient. Surgery fails because it has not been radical enough and local recurrence with or without distant metastasis is the rule. Radiation therapy fails because the tumor is quite radioresistant and the high doses required for its control are beyond the tolerance of uninvolved surrounding tissues. In this case the radium implant offered an ideal solution to the problem of preservation of normal structures while delivering the necessary radiation to the tumor. Since recurrent tumor and/or distant metastasis usually result in the demise of the patient within a 2 year interval from the time of the treatment,[1] it appears that therapy in this case may well have been successful.

* Presented at the Fiftieth Annual Meeting of the American Radium Society, Miami Beach, Florida, April 7–11, 1968.
From the Radiation Therapy Section, Radiology Service, Walter Reed General Hospital, Walter Reed Army Medical Center, Washington, D. C.

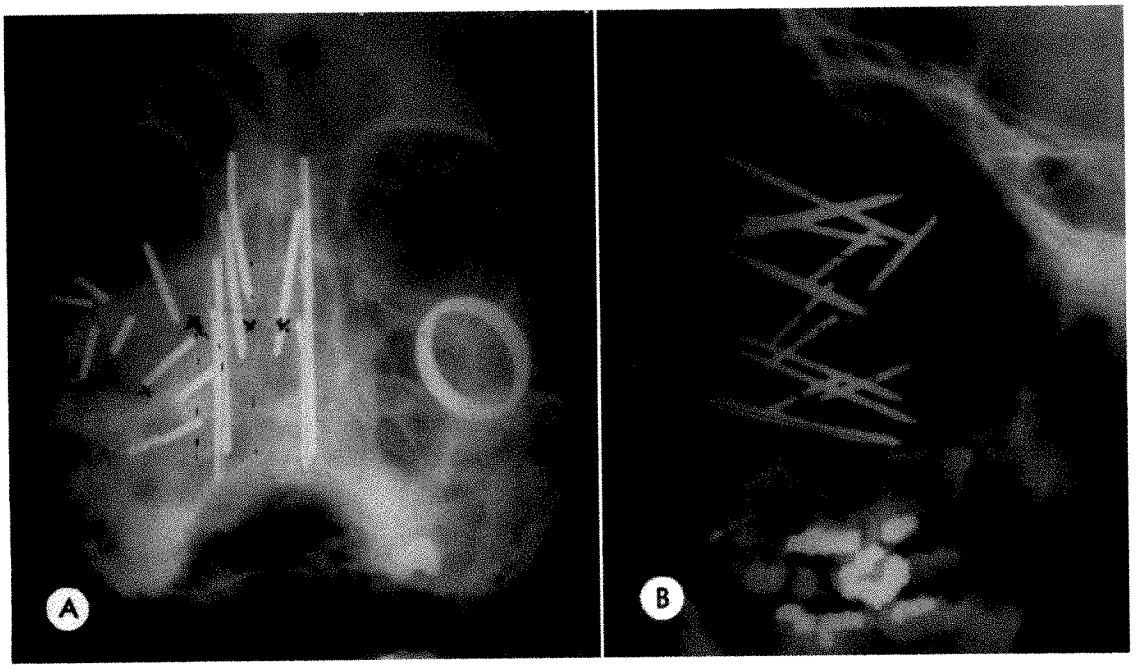


Fig. 1. (*A* and *B*) Case 1. Maxilloethmoidal radium implant. "X" indicates the points arbitrarily chosen for dose calculations. ½

Case II. R. C. is a 19 year old man who had a fungating tumor of the hard palate on the left side (Fig. 2). Biopsy revealed it to be an osteosarcoma. A course of preoperative irradiation by means of an interstitial implantation was planned. Thirty-two low intensity radium needles were placed into the tumor mass as well as into the normal-appearing tissue in the immediate vicinity (Fig. 3, *A* and *B*). A plane of low intensity needles was placed along the external surface of the left maxilla and was included as part of the implant volume. Dosimetry was based on the Quimby schedule for volume implants, and in this manner a calculated dose of 9,830 r was delivered in 94 hours. Total maxillectomy was performed at the time of removal of the implant and a plastic prosthesis was placed in the surgical defect before closure of the wound. The patient tolerated the implantation and the surgical procedure quite well and was discharged from the hospital in good condition.

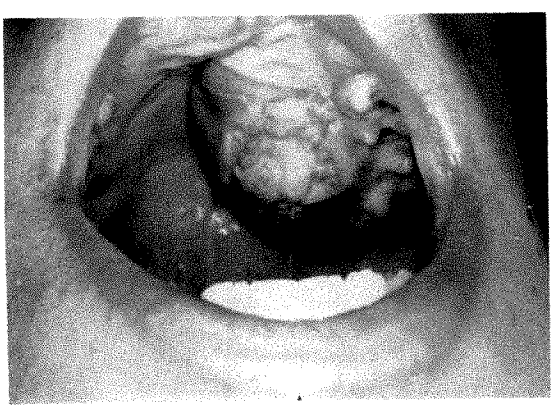


Fig. 2. Case II. Fungating osteosarcoma of the hard palate.

Seven months after the implantation a recurrence was found in the nasal septum and floor of the left orbit, and a course of preoperative interstitial irradiation was again decided upon. Thirty-four low intensity needles were implanted into the areas of recurrence and adjacent normal tissue (Fig. 4, *A* and *B*). A calculated dose of 10,100 r was delivered in 88 hours. Radical surgery, including removal of the left eye, was again performed at the time of removal of the implant. A dental prosthesis was devised and facial reconstruction begun. Six months after this second procedure no evidence of recurrence has been noted, although it is still too early to judge the treatment successful.

Comment. Sarcomas involving the facial bones have considerably less propensity for early distant metastasis than the primary sarcomas occurring in the bones of the ex-

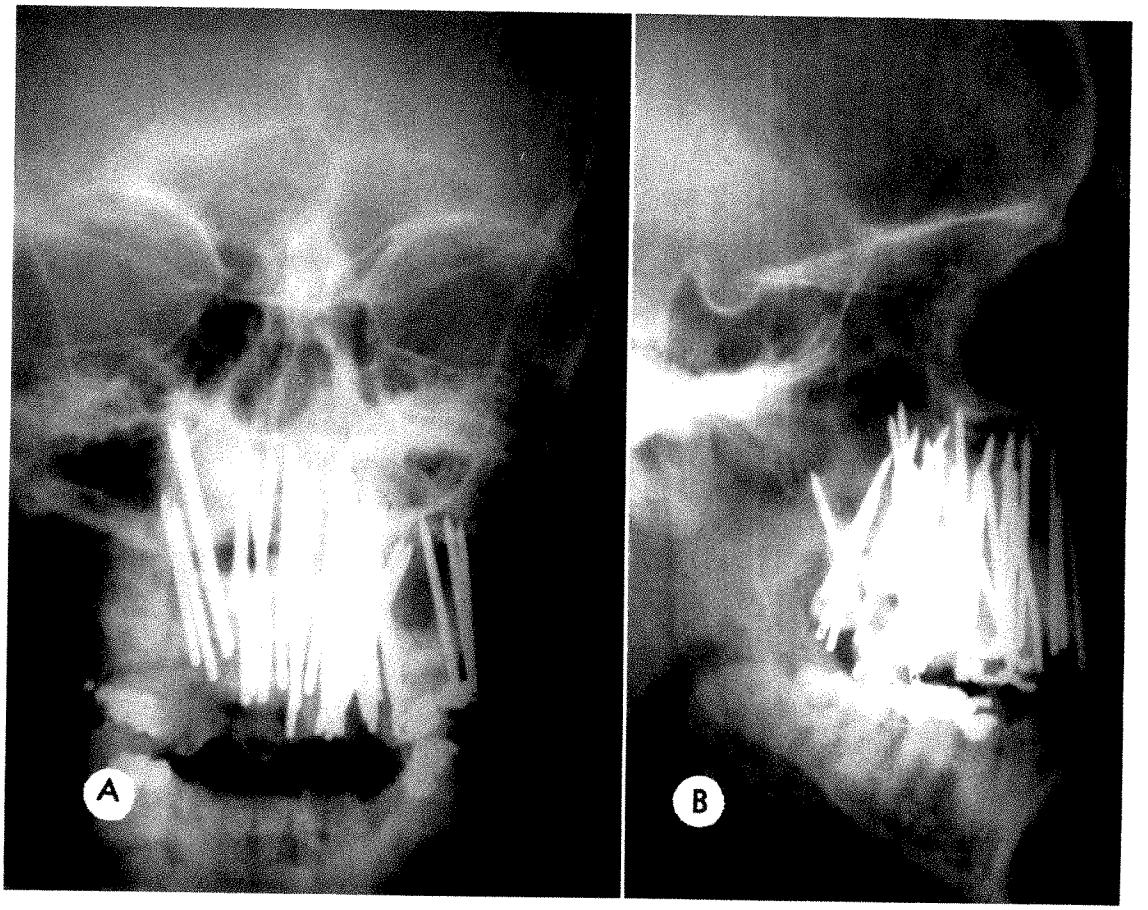


FIG. 3. (*A* and *B*) Case II. Radium implant. Benign lesions are incidentally visible in each side of the mandible.

tremities. Local recurrence is common and ablative surgery remains the treatment of choice where feasible. Encouraged by the results of preoperative, high dose radium implants for osteosarcoma of the mandible,[2] it was decided to attempt such a procedure in this case as a positive effort to reduce the probability of local recurrence. The areas of recurrence which necessitated a second combined procedure occurred in the areas

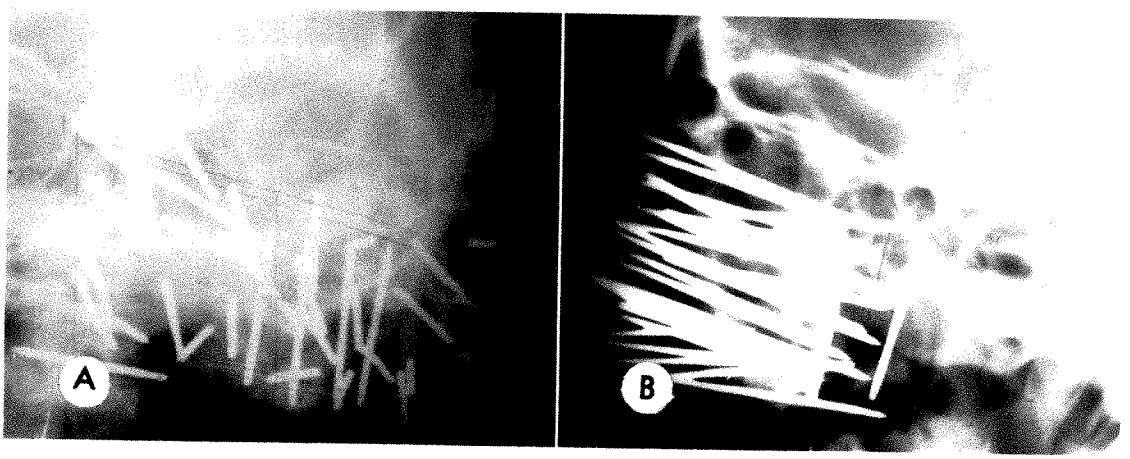


FIG. 4. (*A* and *B*) Case II. Second radium implant.

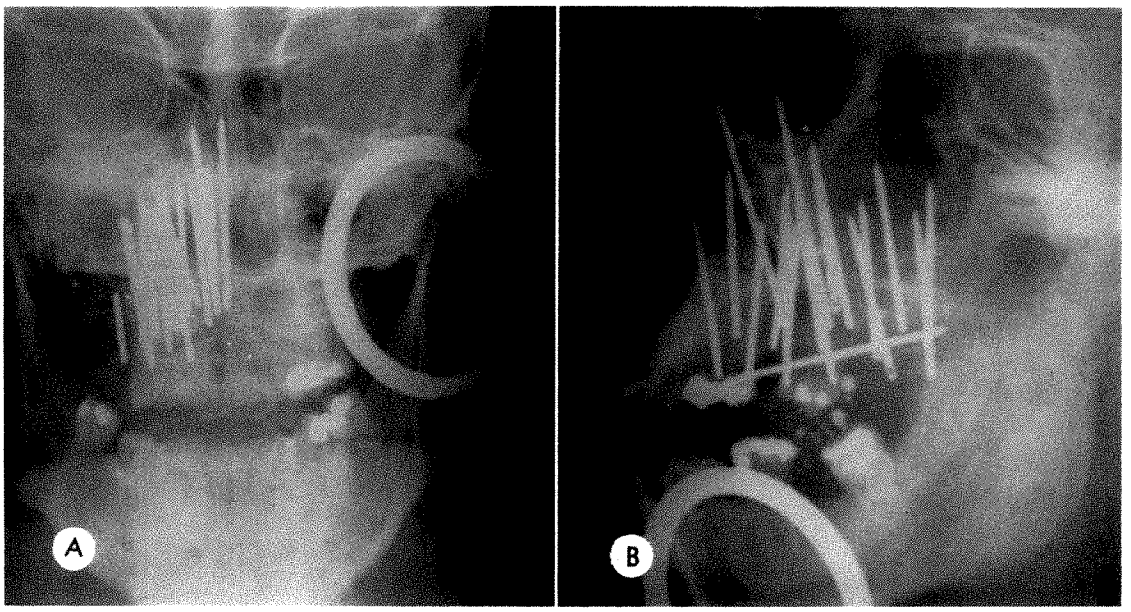


FIG. 5. (*A* and *B*) Case III. Radium implant. Radiopaque globules projected below the implant on the lateral view (*B*) are residua of a sialogram.

just outside of the high dose volume. Definitive surgery was not significantly delayed or compromised in any way.

CASE III. F. G. R. is a 36 year old man who was found to have a tumor involving the right side of the hard palate and maxilla during a routine dental examination. There was a large defect in the lateral wall of the right maxillary sinus, the result of a previous surgical procedure. A 3×4 cm. firm mass on the right hard palate could be seen extending from the alveolar ridge anteriorly to the posterior edge of the palate and just across the midline. The alveolar ridge was replaced by a friable, exophytic tumor and the portion of the tumor within the maxillary antrum was visible directly through the surgical defect. Biopsy of the alveolar ridge showed this tumor to be a mucoepidermoid carcinoma. A course of preoperative irradiation by means of a radium implant was planned. Eighteen low intensity needles were placed within the tumor through the palate (Fig. 5, *A* and *B*). The lateral horizontal needle was placed through the thin lateral lip of the tumor and did not represent an intent to cross the inferior aspect of the volume of the radioactive source. Using the Quimby schedule for volume implants, a calculated dose of 11,800 r was delivered in 92 hours. The two longer vertical needles in the medial location were heavily loaded at the pointed ends (Indian club) in an attempt to deliver some radiation to a questionably involved portion of the anterior ethmoidal sinus. A partial maxillectomy was performed under general anesthesia immediately after the needles were removed and a plastic prosthesis was placed in the surgical wound prior to closure. The implantation and the surgical procedure were well-tolerated and the patient is living and well 13 months post-implantation and surgery with no evidence of recurrence.

Comment. This tumor type accounts for about 25 per cent of malignant salivary gland tumors[1] and probably arose in a minor salivary gland structure in the soft tissues of the palate. As in the preceding cases, there is a tendency for local recurrence after surgery or radiation therapy. The rationale for the implant is again an attempt to eliminate local recurrence as a cause for therapeutic failure.

TECHNIQUE OF IMPLANTATION

The feasibility of radium implantation of the mandible has been documented previously. Implantation of the maxillary and ethmoidal areas is also quite simple technically. The procedures are done under gen-

eral anesthesia. The percutaneous implantation of the ethmoidal sinus area as performed in Case 1 follows the technique used at the University of Maryland.[3] The critical needles are those at the superior aspect of the ethmoidal planes which must be positioned to avoid entering the cranial cavity. Holes are drilled through the nasal cavity and sinuses using an electric orthopedic drill or dental burr. If the caliber of the drill or burr is slightly larger than the diameter of the radioactive needles, no resistance to their placement will be encountered if the needles are made to follow the predrilled path. Bleeding from the nasal fossa is initially brisk but quickly subsides spontaneously. The landmark for the first hole is a point 5 mm. above the midpoint of the inner canthus and 7.5 mm. lateral to the midline of the nasion. The drill is directed on a line parallel to the canthomeatal line. Confirmation of the proposed needle position is obtained from landmarks on roentgenograms. A dummy needle is placed in the predrilled hole and roentgenograms are obtained before proceeding further. After confirming the proper position of the first needle, this dummy needle is then partially withdrawn and serves as a guide for position and direction of the other needles in the implant. Dummy needles are placed in the drill holes immediately after drilling, and roentgenographic confirmation of their position is obtained just prior to their removal and replacement with radioactive needles. As can be seen in Figure 1, *A* and *B*, the superior needles in the ethmoid implant were of 4.5 cm. physical length, but ideally should have been longer. Placement of the high intensity needles in the maxillary sinus presented no particular problem since the surgical debulking procedure provided an excellent opportunity for direct vision. Threads in these needles were brought out through the wound and taped to the cheek. The needles on the floor of the orbit were inserted last. A small incision was made in the skin with a scalpel prior to their insertion in order to avoid the excess pressure on the globe required to push these blunt needles through the skin. The points of the needles were directed inferoposteriorly in an attempt to "scrape" the floor of the orbit.

Dose calculation offers a bit of a challenge and can be done in a number of ways. It was elected in this case to choose a few critical points in the treated volume and find the dose rate at these points. The contribution of each ethmoidal plane to these points was calculated using the Quimby rules for planar implants. Contribution of each of the other needles to the same points was calculated using linear source tables. Because of the large amount of radium in the maxillary antrum, a dose of 2,000 r was delivered in less than half a day.

The technique in the other 2 cases was devised after considering the problem of adequate coverage of the involved volume by percutaneous implantation. Theoretically, this could be done but the configuration of the resulting implant would be less than ideal. Insertion through the palate is better since a cylindrical volume implant is possible and the skin over the sinus is spared both surgical trauma and radiation effects. In Case 11 the dimensions of the tumor allowed the use of 4.5 cm. physical length needles throughout most of the implant. The second implantation in this patient was performed percutaneously, similar in technique to the first case. All of the needles were low intensity and the large volume included the left inferior orbital plate. In the last case, 3 cm. needles had to be used in order to avoid penetration of the base of the skull, since the floor of the anterior fossa is at most 4.5 cm. above the hard palate. Needles are put into place after predrilling a hole in the desired spot with a dental burr. Because of the limited but rather profuse bleeding which occurs when the burr is removed, the operator must keep the burr in place while indicating its direction by partially withdrawing it. An assistant places the tip of the radium needle next to it and noting the proper direction instructs the operator to remove the drill and slips the needle into place immediately before the puncture site is obscured by blood. The posterior needles are placed

first and the remaining needles are evenly placed at intervals of approximately 1 cm. throughout the critical volume. When the most anterior portion of the maxilla is implanted, there may be considerable resistance to the drill when it meets the roots of the upper incisors. If the alveolar ridge is involved in the neoplastic process, (as it was in Case II), a row of needles is placed adjacent to its external surface beneath the mucous membrane of the gum and cheek. Vaseline gauze is placed over the implant and its edges are sutured to the palate and gums. This serves to hold the needles in place until the calculated time of removal.

Tracheostomy was performed prior to the implantation in Cases II and III, since this would be required prior to maxillectomy in any event and does assure an adequate airway at all times. The implantations were accomplished in less than 1 hour of operating time.

DISCUSSION

The two indications for interstitial implantation of the paranasal sinuses and facial bones are: (1) to supplement the maximum tolerable dose of external irradiation to unresectable lesions; and (2) to deliver a large preoperative dose to resectable lesions. Although external radiation therapy could be used in the latter instance, the usual regimen for preoperative irradiation is presently 4,000 to 6,000 r in 3 to 6 weeks with surgery to follow radiation therapy in 4 to 6 weeks. Thus there is considerable delay before the definitive surgical procedure is performed. Although this delay may be unimportant as regards prognosis, a method which eliminates the delay without compromising the results would seem preferable. A smaller dose, volume, and time combination with external irradiation may be equally effective (*e.g.*, 2,000 r in 2 to 3 days using cobalt 60 gamma rays) but has not been investigated, since the possibility of delivering 9,000 to 10,000 r in less than 4 days to radioresistant tumors is more appealing. Theoretically, the radium implant is particularly ideal for small volume, high dose, preoperative irradiation, and, in a limited number of cases thus far, it seems to be effective.

Although implantation in the facial area would at first appear to be a rather formidable procedure, from the standpoint of patient tolerance and operative technique, such is not found to be the case. During the period when the needles are in place, there is remarkably little discomfort to the patient. Eating is a problem, but fluids can be controlled intravenously for the few days in question. The surgical technique is not altered in any way by the implant since the late fibrous radiation reaction is not given a chance to develop. The most heavily irradiated tissues are completely removed.

CONCLUSIONS AND SUMMARY

1. Interstitial radium implantation of the facial structures is a practical therapeutic procedure.

2. The procedure is of particular value in the treatment of malignant diseases in this area which are considered to be radioresistant and prone to local recurrence after treatment. Specific indications are:

   a. Inoperable lesions—to supplement the maximum tolerated dose of external irradiation.

   b. Operable lesions—to deliver preoperatively a high dose of irradiation to the involved volume in the shortest possible time.

3. The effect of this therapy on the prognosis of patients with these lesions will be difficult to document because of their uncommon occurrence. The preliminary results have been encouraging.

Carl W. Boyer, Jr., Lt. Colonel, MC, USA
Radiation Therapy Section
Box 329 Tripler General Hospital
APO San Francisco, California 96438

REFERENCES

1. ACKERMAN, L. V., and DEL REGATO, J. A. Cancer: Diagnosis, Treatment, and Prognosis. Third edition. C. V. Mosby Company, St. Louis, 1962, p. 252, 718.

2. BOYER, C. W., JR., BRICKNER, T. J., JR., and WRATTEN, G. P. Treatment of osteogenic sarcoma of mandible. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1967, *99*, 326–332.

3. WEISENBERG, M. Personal communication.

COMBINED INTRA-ARTERIAL INFUSION AND RADIOTHERAPY FOR THE TREATMENT OF ADVANCED CANCER OF THE HEAD AND NECK*

By RICHARD H. JESSE, M.D., HELMUTH GOEPFERT, M.D., ROBERT D. LINDBERG, M.D., *and* ROBERT H. JOHNSON, M.D.
HOUSTON, TEXAS

REGIONAL chemotherapy administered by the protracted intra-arterial infusion of antimetabolites has been available to surgeons for one decade. Sullivan *et al.*[9], Watkins and Sullivan,[10] Rogers,[7] and Johnson and colleagues[4] have been impressed with the ability of the antimetabolites to shrink the size of the cancer or to make it regress completely. In the latter series[4] the malignant cells were still microscopically present at the conclusion of the infusion. In a previous publication[3] the present authors indicated that the results of infusing antimetabolites in large cancers were disappointing and that the degree to which the patient is benefited is often outweighed by the morbidity and mortality resulting from the procedure.

Spurred on by the report of Foye *et al.*[2] in which a potentiation of radiation damage to the cancer cell by 5-fluorouracil was indicated, the present authors became intrigued with attempting this treatment for patients with carcinoma of the head and neck. When Langdon and his coworkers[5] in 1962 reported that patients with lung cancer treated by systemic chemotherapy and radiation therapy failed to survive longer than those treated by radiation therapy alone, we decided to use the intra-arterial method for delivering the drug. The results of this pilot study are herein presented.

MATERIAL AND METHOD

Forty-six patients with locally advanced cancers of the head and neck received a chemotherapeutic agent intra-arterially and concomitant radiation therapy in the years 1962 to 1966. All patients, with one exception, were considered incurable by the consensus of the surgeon and radiotherapist. A patient with a relatively small lesion of the floor of the mouth who refused surgical therapy was the exception.

To administer the chemotherapeutic drug a polyvinyl catheter* is placed in one or both external carotid arteries. The superficial temporal artery is the usual route of insertion and local anesthesia is employed. An extensive dissection to straighten out the superficial temporal artery is usually necessary before the catheter can slide into it easily. If large obstructing lymph nodes or an extremely tortuous temporal artery make retrograde catheterization impossible, a direct cut-down on the superior thyroid branch of the external carotid artery is necessary. The distribution of infusate is determined by observing the intensity of the dye in the tumor area as seen under a Wood's lamp while slowly injecting 20 per cent fluorescein dye into the catheter.

The chemotherapeutic drug is administered in 500 cc. of quarter strength saline to which has been added 1,000 units of heparin. The infusion pump is calibrated to administer 500 cc. in a 24 hour period. The patient receives the infusion on Days 1–5 inclusive and on Days 7–12 inclusive. A dose of 200 rads radiation is administered on Days 2–6 inclusive and Days 8–13

* Abbott Venocath 18.

* Presented at the Fiftieth Annual Meeting of the American Radium Society, Miami Beach, Florida, April 7–11, 1968.
From the Department of Radiotherapy, The University of Texas M. D. Anderson Hospital and Tumor Institute at Houston, Houston, Texas.
Supported in part by the American Cancer Society, Texas Division.

inclusive. On the thirteenth day the catheters are withdrawn. The radiation therapy is continued at the rate of 1,000 rads a week for a total dose of 6,000 to 7,000 rads.

The antimetabolites employed have been methotrexate and 5-fluorouracil. Nine patients treated earlier in the series received methotrexate, since the authors had a wide experience with this drug. Twenty-five patients treated later in the series received 5-fluorouracil. The dose of methotrexate



FIG. 1. Cancer of gum. (*A*) Intraoral view. (*B*) Extension to skin.



FIG. 2. Squamous cell carcinoma of the gum with extension to the left mandible.

administered was 25 mg. if 1 catheter was employed, or 50 mg. if bilateral catheterization was necessary. Citrovorum factor was administered intramuscularly at a ratio of 1 mg. citrovorum to 2 mg. methotrexate. The total amount of methotrexate the 9 patients received individually varied from 250 to 700 mg.; the average patient receiving 410 mg.

The daily dose of 5-fluorouracil was 4 or 8 mg./kg. depending on whether 1 or 2 catheters were employed. The total individual dose ranged between 2,500 and 12,000 mg., with the average patient receiving 5,000 mg.

A typical patient case history follows.

REPORT OF A CASE

J. F., a 65 year old man, was referred to the M. D. Anderson Hospital and Tumor Institute in July, 1963 because of a squamous cell carcinoma of the floor of the mouth which extended through the mandible and the submental soft tissue, ulcerating the skin (Fig. 1, *A* and *B*; and 2). Through the catheters in the superficial temporal arteries bilaterally the patient received 7 gm. 5-fluorouracil within 12 days. Five thousand rads cobalt 60 teletherapy was administered in 4 weeks. The tumor rapidly responded to this treatment, with the only side effect being a moderate mucositis of the oral

P24,921

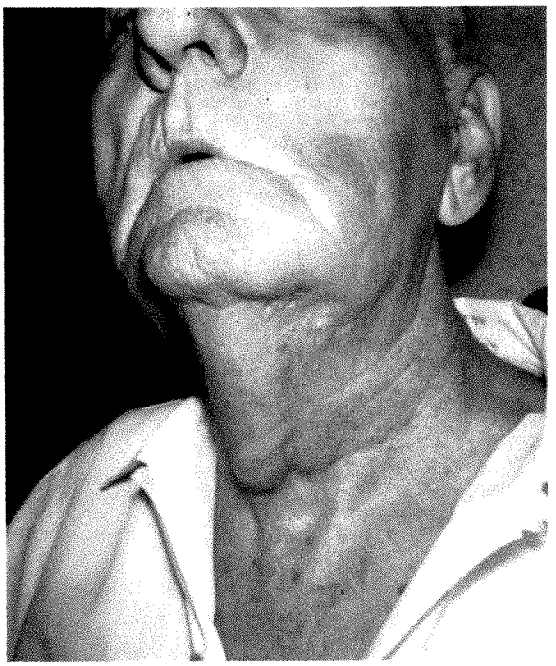


FIG. 3. Four weeks following combined therapy, the skin lesion has cleared.

cavity (Fig. 3; and 4). During the following months, recalcification of the mandible occurred. The patient was free of disease 4 years after the treatment.

RESULTS

This report will analyze the effectiveness of therapy in 34 of the 46 patients who completed the infusion and also received a cancerocidal dose of radiation therapy. Therapy was not completed in the remaining 12 patients because of severe local toxicity, distant metastasis appearing during therapy, or the patient's desire to stop the treatment: they are excluded from the analysis.

Twelve of the 34 patients (35.3 per cent) have had no local recurrent cancer as shown in Table I. These patients have been followed between 8 and 60 months with a median of 33 months after completion of treatment. This is not to imply, however, that all of these 12 patients are still living and well, since only 5 of them satisfy this status as indicated in Table II. Four of the patients have had regional or distant metastasis, 3 of whom are dead of the cancer and 1 who has not yet expired of this disease. Two of the patients have had a second primary cancer, one dying of carcinoma of the esophagus 29 months after completion of the head and neck treatment, the other living 60 months with an astrocytoma. One patient in the group died at 37 months of a coronary occlusion.

Ten of the 34 patients (29.4 per cent) developed recurrent cancer in the treated area between 4 and 42 months (median 13 months) after completion of the treatment, and their status is summarized in Table III. Seven of these patients are dead of their cancer or of the complications of a secondary treatment. The three additional patients had had a surgical excision of the recurrent lesion and are living; 1 as long as 24 months after the secondary treatment.

Of the 34 patients, 10 were designated as failures since their local cancer was never eradicated, and all have expired of their cancer. Two additional patients could not be evaluated and are also considered treatment failures. One of these patients died of an unrelated cause only 3 months after the treatment and the other was lost to follow-up.



FIG. 4. The intraoral tumor has responded well to the combined therapy. There is only a moderate mucositis present.

TABLE I

CONCOMITANT CHEMOTHERAPY + RADIOTHERAPY
(34 Patients)

	No. of Patients	Per Cent of Total	Time in Months	Median Time in Months
No local recurrence	12	35.3	8–60	33
Local recurrence	10	29.4	4–42	13
Failure	12	35.3	—	—

The superiority of one chemotherapeutic agent over another cannot be significantly stated since the number of patients in the 2 groups is too small. The analysis shown in Table IV appears to indicate that 5-fluorouracil is somewhat superior.

Of perhaps more interest is the analysis of the local recurrence in relationship to the site of the original lesion which is summarized in Table V. Over 40 per cent of the patients whose primary lesion originated in the oral cavity, sinus and skin, were free of local cancer. Of 6 patients with cancer of the oropharynx, local control of the disease was not obtained.

DISCUSSION

Fletcher and Jesse[1] reported that 5-fluorouracil administered systemically during radiation therapy did not alter the longterm survival of the patient; however, the cancer regressed more rapidly. Since a greater concentration of the drug can be delivered to the tumor area by the intra-arterial route of administration, it is felt that this might be advantageous, but it is also realized that there are limitations of the intra-arterial method of administration. Nahum[6] has described the relationship that the blood supply has to the area

TABLE II

STATUS OF 12 PATIENTS WITH NO LOCAL RECURRENCE

Time in Months Since Infusion	Status*
60	Second primary in brain, living
58	NED
48	NED
39	NED
37	Dead—OC
33	Dead—DM
33	NED
29	Dead—second primary
19	Dead—DM
18	NED
14	LWM
8	Dead—DM

* NED—No evidence of disease; DM—distant metastasis; OC—dead of other causes; LWM—living with metastasis.

TABLE III

STATUS OF 10 PATIENTS WITH LOCAL RECURRENCE

Time Recurrence in Months	Secondary Treatment	Result*
4		DOD 13 months
4		DOD 7 months
6		DOD 19 months
7		DOD 22 months
13		DOD 14 months
13	Surgical excision	NED 37 months
15		DOD 18 months
20	Au^{198} implant	DOC 31 months
21	Surgical excision	NED 36 months
42	Surgical excision	NED 44 months

* DOD—Dead of cancer; NED—no evidence of disease; DOC—dead of other causes.

TABLE IV

SURVIVAL *versus* AGENT EMPLOYED

Agent	No Local Recurrence
Methotrexate (9)	2
5-Fluorouracil (25)	10

TABLE V

CANCER LOCATION *versus* RECURRENCE

Location	No. of Patients	No Local Recurrence
Oral cavity	23	9
Maxillary antrum	4	2
Tonsillar fossa, palate, pharynx	6	0
Skin, scalp	1	1
Total	34	12

of the cancer that is covered by the infusion. The cancers confined to the intraoral and sinus areas are generally covered by a catheter low in the external carotid artery, while oropharynx cancers are likely to have part of the blood supply coming from the subclavian artery and, therefore, not be totally infused. This could explain, therefore, why the cancers of the oropharynx were not eradicated by this combination treatment. Rush *et al.*[8] have indicated that complete mixing of the infusate and the blood does not always occur at the tip of the catheter unless it is injected under some force. Since the present method uses a low volume, delivered with little force, mixing may occur at a level distal to the tip of the catheter. Determining the distribution of infusate by colorimetric means is a gross test. Only by obtaining histochemical determinations of multiple biopsy specimens or by scanning the tumor after using radioactive tracer in the infusate could quantitative concentration titers be determined.

The concomitant use of the chemotherapeutic agent and radiation therapy was chosen over the sequential use of the two modalities for this study; partly empirically and partly to rid the experiment of another variable. Johnson *et al.*[4] have shown that if the chemotherapeutic agent is delivered to the cancer for 2 to 3 weeks prior to the radiation therapy, a significant amount of tumor regression is produced in many patients. It is difficult to determine clinically whether the rapid regression of cancer after the sequential treatment is because of a sensitizing effect of the chemotherapeutic agent on the cancer cell or whether the drug decreases the total amount of cancer, thereby increasing tissue oxygenation and the effectiveness of the radiotherapy. If the effect of the drug on the cell is truly one of sensitization to radiation therapy, this should occur during concomitant treatment.

The complications encountered by the concomitant use of these treatment modalities have varied in their severity. Patients exhibit a wide range of individual sensitivity to methotrexate even though their measurable kidney and liver reserves appear to be the same. In those patients treated with methotrexate there was usually a moderate local toxicity starting about the seventh infusion day. A systemic toxicity with a leukopenia and thrombocytopenia was usual during the second week of treatment.

The toxicity from 5-fluorouracil was universally limited to the local area; no general manifestations of the drug were apparent. There was generalized erythema of the skin and mucosa starting about the fourth or fifth infusion day. This rapidly progressed to patchy ulceration both of the skin and the mucosa in some patients. Moist desquamation and necrosis of the skin and cartilage of the external ear were occasionally seen. Depapillation of the tongue which persisted for life was seen in those patients whose tongue was included in the infusion.

While analyzing those patients who were not controlled, two disturbing factors were noted. First, there were 2 patients with late local recurrence, one at 21 months and one at 42 months after the treatment. The concomitant treatment may cause a tremendous scar tissue in which cancer cells are trapped, but viable; a reasonable assumption since the local tissue reaction is greater than with irradiation alone.

The second disturbing factor was that 33 per cent of the patients who had no local recurrence developed distant metastasis. One expects more distant metastases in patients as the local control rate rises, since more of them are exposed to this risk, but the 33 per cent figure seems quite high. A change in the host-tumor relationship in the nonirradiated areas of the body brought about by the chemotherapy, might be an explanation.

SUMMARY AND CONCLUSION

Thirty-four of 46 patients were able to complete a course of concomitant intra-arterial chemotherapy and radiation ther-

apy for locally far advanced cancer of the head and neck. Twelve of the 36 patients had no local recurrence although some of these died of distant metastases, second primary malignant neoplasms, and other causes. Ten of the patients had a complete disappearance of the lesion only to have it recur later. The remaining 12 patients had no local control of their cancer or were unavailable for follow-up. Eight of the 34 patients are living free of their disease 18 months or more after completion of therapy. Patients in whom the entire cancer was in the distribution of the external carotid artery are the only survivors. It is felt that this pilot program has produced more success in the local control of cancer than would normally be expected if chemotherapy had not been employed. A carefully controlled series will be necessary to assess the value of this approach.

Richard H. Jesse, M.D.
Department of Surgery
The University of Texas
M. D. Anderson Hospital and Tumor Institute at Houston
Houston, Texas 77025

REFERENCES

1. Fletcher, G. H., and Jesse, R. H., Jr. Contribution of supervoltage roentgenotherapy to integration of radiation and surgery in head and neck squamous cell carcinomas. *Cancer*, 1962, *15*, 566–577.
2. Foye, L. V., Jr., Willett, F. M., Hall, B., and Roth, M. Potentiation of radiation effects with 5-fluorouracil. *Cancer Chemother. Rep.*, 1960, *6*, 12–15.
3. Jesse, R. H., Villarreal, R., Letayf, V., Rufino, C., and Hickey, R. C. Intra-arterial infusion for head and neck cancer. *A.M.A. Arch. Surg.*, 1964, *88*, 618–627.
4. Johnson, R. O., Kisken, W. A., and Curreri, A. R. Squamous cell carcinoma of oral cavity: intra-arterial infusion with fluorouracil and idoxuridine. *A.M.A. Arch. Surg.*, 1965, *90*, 760–763.
5. Langdon, E. A., Ottoman, R. E., Rochlin, D. B., and Smart, C. R. Early results of combined radiation and chemotherapy in treatment of malignant tumors. *Radiology*, 1963, *81*, 1008–1013.
6. Nahum, A. M. Limitations imposed by head and neck vasculature on regional chemotherapy. *Surg., Gynec. & Obst.*, 1963, *116*, 539–546.
7. Rogers, D. S. Cancer chemotherapy by continuous intra-arterial infusion. *Cancer*, 1964, *17*, 1365–1380.
8. Rush, B. F., Jr., Horie, N., and Klein, N. W. Intra-arterial infusion of head and neck: anatomic and distributional problems. *Am. J. Surg.*, 1965, *110*, 510–513.
9. Sullivan, R. D., Miller, E., and Sikes, M. P. Antimetabolite-metabolite combination cancer chemotherapy: effects of intra-arterial methotrexate intramuscular citrovorum factor therapy in human cancer. *Cancer*, 1959, *12*, 1248–1262.
10. Watkins, E., Jr., and Sullivan, R. D. Cancer chemotherapy by prolonged intra-arterial infusion. *Surg., Gynec. & Obst.*, 1964, *118*, 3–19.

CANCER OF THE BASE OF THE TONGUE*

116 PATIENTS TREATED RADIOTHERAPEUTICALLY IN THE 11 YEAR PERIOD 1952 THROUGH 1962

By PAUL W. SCANLON, M.D.,† EDWARD H. SOULE, M.D.,‡ KENNETH D. DEVINE, M.D.,§ *and* JAMES B. McBEAN, M.D.‖
ROCHESTER, MINNESOTA

TWO previously published studies—142 cases of carcinoma of the nasopharynx and 131 cases of carcinoma of the tonsil treated in the years 1950 through 1960—were made in an attempt to evaluate the results of major changes occurring in radiotherapeutic practice at the Mayo Clinic in this 11 year period. These changes were essentially: (1) a change to higher orthovoltage dosages in the earlier years of the period; (2) the advent of cobalt 60 teletherapy in 1954; and (3) the advent of split-dose techniques in 1958. The present study of 116 cases of cancer of the base of the tongue completes the triad of naso-orohypopharyngeal cancers commonly considered to be almost exclusively in the radiotherapeutic domain. We feel that this triad is especially suitable for an assessment of changes in radiotherapeutic techniques, since the bias in selection of patients for radiotherapy is minimal.

MATERIAL AND METHOD

We reviewed the data on 116 patients with cancer of the base of the tongue who received their primary definitive treatment at the Mayo Clinic in the years 1952 through 1962. We excluded those whose disease was diagnosed primarily at the Mayo Clinic but who subsequently went elsewhere for therapy, and also those who had been treated previously elsewhere and had come to the Mayo Clinic for an opinion on the management of recurrent cancer. We included all those who received their primary definitive therapy here, even a few who received radiotherapy in very modest amounts because of an obviously near-terminal condition. Patients with lymphoma of the base of the tongue were included only if the disease was limited to the region above the clavicles. It may be well at this point to explain a departure from the commonly accepted line of demarcation for inclusion of cancers that may truly be designated lesions of the base of the tongue. Instead of the line of the circumvallate papillae used by others as the dividing line, we chose to include and classify as lesions of the base of the tongue all primary lesions posterior to the anterior faucial pillars. If the bulk of the primary cancer occurred opposite the fauces with only minimal extension anteriorly, we considered this truly a lesion of the base of the tongue. Contrariwise, if the predominant bulk of the lesion appeared in the anterior dorsum of the tongue, the lateral margin of the tongue, the retromolar trigone, or floor of the mouth, with only minimal extension into the posterior aspects of the tongue, we excluded it from consideration.

SEX AND AGE DISTRIBUTION

The ratio of males to females was 3.8:1 (Table 1). This male predominance is in accord with that of most other reported series. Most patients (86 per cent) were in the sixth, seventh, and eighth decades of life. This age spread subtended 89 per cent of the 5 year survivors. The median age was 62 years.

While it would appear from Table 1 that females had a somewhat better survival rate than males—a selectivity in head and

* Presented at the Fiftieth Annual Meeting of the American Radium Society, Miami Beach, Florida, April 7–11, 1968.
From the Mayo Clinic and Mayo Foundation: Section of Therapeutic Radiology,† Surgical Pathology,‡ Plastic Surgery,§ and Otolaryngology and Rhinology.‖

neck cancer often reported by others—the difference is not statistically significant. There likewise seems to be no preferential effect of age on survival rates.

PRESENTING SYMPTOMS

Data on presenting symptoms are given in Table II. Unlike patients with cancer of the nasopharynx, where one may encounter a bewildering array of presenting symptoms, patients with cancer of the base of the tongue usually present with pain or some unpleasant sensation directly attributable to the primary lesion, interference with deglutition or other basic functions of the tongue, or metastatic lymphadenopathy in the neck. We attempted to ascertain whether any one presenting symptom carried a more ominous prognosis than the others, but such was not found to be the case.

DURATION OF PRESENTING COMPLAINTS

It would appear that patients presenting with symptoms of relatively brief duration, implying discovery at an early stage of the disease, fared somewhat better than those with symptoms of longer duration (Table III). Again, however, the differences are not statistically significant and one cannot say with certainty that duration of symptoms is in any way related to survival.

TABLE I

RELATIONSHIP OF SEX AND AGE TO SURVIVAL
(116 Patients)

	Patients	
	No.	Survived 5 Yr. (per cent)
Sex		
Male	92	27
Female	24	42
(M:F ratio 3.8:1)		
Age (yr.)		
21–30	1	—
31–40	1	—
41–50	11	27
51–60*	38	29
61–70*	37	30
71–80*	25	36
> 80	3	—

* The age group 51–80 years represents 86 per cent of the patients and 89 per cent of the 5 year survivors.

TABLE II

PRESENTING SYMPTOMS

Symptom	Patients		
	No.	Per Cent of 116	Survived <5 Yr. (per cent)
Sore throat or foreign-body sensation	79	68	65
Cervical lymph nodes enlarged	51	44	75
Dysphagia or pain associated with swallowing, acidity, or temperature change	48	41	71
Pain in ear, jaw, neck, head, or face	32	28	69
Visible or palpable tumor in base of tongue	23	20	78
Hoarseness	17	15	77
Hemoptysis	12	10	67
Cough or wheeze	8	7	75
Weight loss	6	5	—
Excessive salivation or "phlegm"	4	3	—
Dysarthria	4	3	—
Fever or chills	3	3	—
Miscellany (1 each of fatigue, loss of taste, weakness and anemia, hearing loss, paralysis of tongue)	5	4	—
No complaint—cancer found on routine examination	2	2	—

PATHOLOGIC CLASSIFICATION

The pathologic classification of the 116 cases is presented in Table IV. As expected, the great majority of the tumors proved to be squamous cell carcinoma (78 per cent). A little more than a third of the squamous cell carcinomas were of Grade 1 or 2 (Broders' classification), in contrast to slightly less than two-thirds that were of Grade 3 or 4. There was no statistically significant dif-

TABLE III

RELATIONSHIP OF DURATION OF PRESENTING COMPLAINT TO SURVIVAL

Duration of Complaint (mo.)	Patients	
	Total*	Survived 5 Yr. (per cent)
<3	67	39
3–5	20	20
6–11	9	22
≧12	18	28

* Patients in each category for whom complaint was recorded.

ference in survival rates according to grade of squamous cell carcinoma. The 5 year survival rate was 26 per cent for patients with squamous cell carcinoma in contrast to 39 per cent for those with lymphomas. The apparently better survival of patients in the miscellaneous group is probably not meaningful considering that the group contains 6 cylindromas and 1 mucoepidermoid carcinoma—tumors renowned for their indolent growth and long clinical course.

RELATION OF LOCATION OF PRIMARY LESION TO INVASIVENESS AND CURABILITY

It is generally agreed that the gross appearance of primary tumors of the base of the tongue has little to do with either their histologic classification or their subsequent curability. Yet it is equally obvious that the degree of local extension and dissemination to regional lymph nodes is of paramount importance in the eventual outcome of treatment.

Table v reflects the relation of local and regional dissemination to 5 year curability rates. Lesions limited to the true base of the tongue have the best prognosis, but the salvageability in such cases (5 year cure rate of 48 per cent) was not as great as in cases of truly limited tonsillar cancer (5 year cure rate of 68 per cent) or limited nasopharyn-

TABLE IV

PATHOLOGIC CLASSIFICATION

Category	Patients		
	Total	Per Cent of 116	Survived 5 Yr. (per cent)
Squamous cell carcinoma	90	78	26
Grades 1 and 2	34	29	29
Grades 3 and 4	56	48	23
Lymphoma	13	11	39
Lymphoblastic lymphosarcoma	6		
Lymphocytic lymphosarcoma	5		
Mixed cell lymphosarcoma	1		
Reticulum cell sarcoma	1		
Lymphoepithelioma	2	2	50
Miscellany	11	9	55
Grade 4 undifferentiated carcinoma	2		
Cylindroma	6		
Adenocarcinoma	2		
Mucoepidermoid carcinoma	1		
Total	116	100	—

TABLE V

RELATIONSHIP OF DISSEMINATION OF BASE OF TONGUE CANCER TO CURABILITY

Location	Patients		
	Total	Per Cent of 116	Survived 5 Yr. (per cent)
Limited to base of tongue	21	18	48
Extension to:			
Lateral hypopharyngeal wall	22	19	41
Tonsil or palate	24	21	29
Anterior tongue or floor of mouth	12	10	25
Valleculae, epiglottis, or pyriform fossa	30	26	23
Cervical lymph nodes	81	70	24
Ipsilateral	61	53	28
Small mobile (N1)	29	25	35
Large fixed (N2)	32	28	22
Contralateral or bilateral	20	17	10
Small mobile (N1)	4	3	50
Large fixed (N2)	16	14	0

geal cancer (5 year cure rate of 56 per cent). Whether this reflects a more relentless course of lesions of the base of the tongue or simply the clinician's inability to detect regional dissemination from lesions of the base of the tongue is uncertain. While extension to the lateral hypopharyngeal wall apparently did not greatly alter curability, extension inferiorly into the neighboring valleculae, base of the epiglottis, or pyriform fossa, and likewise extension into the anterior part of the tongue or floor of the mouth, decreased the 5 year salvageability appreciably.

Seventy per cent of the 116 patients had metastatic lymphadenopathy on initial examination. Estimation of the effect of unilaterality of the involved lymph nodes on the cure rate is fraught with many chances of error, especially for a bulky lesion involving both sides of the base of the tongue; but we attempted nevertheless to assay the effect of unilaterality as well as size and fixation of the involved lymph nodes. From Table v it can be seen that small, relatively unfixed, metastatically involved lymph nodes apparently indicate a better prognosis than do large fixed lymph nodes (5 year survival rates of 35 per cent *versus* 22 per cent for ipsilaterally involved lymph nodes and 50 per cent *versus* 0 per cent for contralaterally or bilaterally involved lymph nodes). The 5 year survival rate for patients with metastatic lymphadenopathy on the same side as the bulk of the primary lesion was 28 per cent, in contrast to 10 per cent for those with either contralateral or bilateral lymph node involvement.

T-N-M CLASSIFICATION

The American Joint Committee for Cancer Staging and End Results Reporting at the time of this writing had not yet formulated the T-N-M classification for lesions of the base of the tongue. Consequently, we attempted to simulate the T-N-M classification already accepted for other cancers of the head and neck. In other words, T1 refers to small lesions (less than 2.5 cm. in diameter) confined to the base of the tongue,

TABLE VI

CLASSIFICATION OF PATIENTS BY STAGE OF DISEASE

A. Correlation of T-N-M System and Stage (116 patients)*

	T1	T2	T3
	Stage I	Stage II	
N0	L 5 D 4	L 5 D 7	L 8 D 6
	Stage III		
N1	L 1 D 4	L 2 D 6	L 5 D 11
	Stage IV		
N2	L 3 D 7	L 3 D 12	L 3 D 22

Total, all stages: L 35 (30 per cent)
D 81†

B. Survival According to Stage of Disease

Stage	Total Patients	Survived 5 Yr.	
		No.	Per Cent
I	9	5	56
II	26	13	50
III	29	8	28
IV	50	9	18
Total	116†	35†	30

* L = living 5 yr. or longer; D = dead in less than 5 yr.; per cent denotes 5 yr. survival rate.

† Two T3 N2 M1 cases, both D, not included in above breakdown.

T2 indicates lesions from 2.5 cm. in diameter up to massive involvement of the entire base of the tongue, but without dissemination to the neighboring structures, and T3 indicates lesions that have invaded or disseminated into neighboring structures such as the adjacent epiglottis, lateral hypopharyngeal wall, fauces, palate, anterior part of the tongue, or other intraoral structures. N0 indicates freedom from metastatic lymphadenopathy, N1 indicates the presence of 1 or 2 small, mobile, as yet unfixed metastatically involved lymph nodes confined to one side of the neck, and N2 indicates the presence of large, semifixed or fixed, metastatically involved lymph nodes in either one or both sides of the neck.

Table VI gives the T-N-M breakdown of the 116 cancers of the base of the tongue. The 5 year survival was 56 per cent for patients with Stage I cancer, 50 per cent for Stage II, 28 per cent for Stage III, and 18 per cent for Stage IV, with an over-all rate of 30 per cent.

METHODS AND RESULTS OF TREATMENT

Although individualization is a *sine qua non* of treatment of most head and neck cancers, we felt that from a therapeutic standpoint the 116 patients with cancer of the base of the tongue could be placed in 3 main groups: (1) 68 patients receiving conventional continuous external radiotherapy and treated mainly in the earlier years of the period represented; (2) 34 patients receiving external radiotherapy by split-dose methods and treated predominantly in the latter years of the period; and (3) 14 patients treated predominantly by electrocautery methods, usually supplemented with implantation of radon seeds either with or without accompanying radical neck dissection.

From Tables VII and VIII it can be seen that the 5 year survival rates according to the 3 methods of treatment were remarkably similar. It should not be inferred that external radiotherapy was the only method of treatment in many of the cases in Groups 1 and 2. Frequently, supplemental treatment was employed, which often obscures the effectiveness of the external radiotherapy. Table IX indicates the frequency of the supplemental measures applied in both the treatment failures and the treatment successes in the first 2 groups of patients. In many radiotherapeutic centers it is common practice, for instance, to insert radon seeds or needles in small residual cancers remaining either after completion of a course of external radiotherapy or at some later

Table VII

CLASSIFICATION OF PATIENTS BY TYPE OF TREATMENT*

	Group 1			Group 2			Group 3		
	T1	T2	T3	T1	T2	T3	T1	T2	T3
No	L 2	L 5	L 5	L 1	L 0	L 1	L 2	L 0	L 2
	D 1	D 3	D 5	D 1	D 2	D 1	D 2	D 2	D 0
N1	L 0	L 2	L 1	L 1	L 0	L 4	L 0	L 0	L 0
	D 2	D 2	D 7	D 1	D 2	D 3	D 1	D 2	D 1
N2	L 1	L 1	L 3	L 2	L 2	L 0	L 0	L 0	L 0
	D 2	D 8	D 15	D 5	D 3	D 5	D 0	D 1	D 2

Two T3 N2 M1-D cases not included in above breakdown.

5 Yr. Survival Rate		5 Yr. Survival Rate		5 Yr. Survival Rate	
Stage	Per Cent	Stage	Per Cent	Stage	Per Cent
I	67	I	50	I	50
II	56	II	25	II	50
III	21	III	45	III	0
IV	17	IV	24	IV	0
Total	29	Total	32	Total	29

* Group 1: Conventional continuous external radiotherapy.
Group 2: Split-dose external radiotherapy.
Group 3: Electrocautery excision, radon seeds, with or without radical neck dissection.

date for residual or recurrent cancer. Table IX shows that these supplemental measures were employed with about equal frequency in both the treatment successes and the treatment failures, and it is therefore relatively impossible to assess the contribution of such supplemental measures to the effectiveness of treatment. The same might be inferred for the supplemental surgical measures employed. Simple excision or electrocautery of the primary lesion prior to radiotherapy or more complicated surgical endeavors, such as the commando type of *en bloc* excision of the primary lesion, the hemimandible, and the regional lymph nodes in the neck, were utilized with approximately equal frequency in both the treatment successes and the treatment failures.

Unlike the previously reported nasopharyngeal and tonsillar series, in the present series we could detect no superiority in the end results of treatment by split-dose methods (Table VIII). It may be that improvement with split-dose treatment was masked by the inclusion of a greater percentage of advanced cancers in this group (82 per cent in Stage III or IV *versus* 66 per cent in Stage III or IV in the continuously treated patients), or it may be that the previously reported superiority of end results noted in the treatment of tonsillar and nasopharyngeal cancer by split-dose methods was due to chance or bias in selection of cases. In any event, with the combined experience in this triad of naso-orohypopharyngeal cancers, it should be apparent that split-dose methods are in no way inferior to conventional continuous radiotherapy; and with the definitely lessened morbidity and ease

TABLE VIII

RELATIONSHIP OF TYPE OF TREATMENT TO SURVIVAL

Type of Treatment	Patients		
	Total	Survived 5 Yr.	
		No.	Per Cent
Continuous conventional radiotherapy	68	20	29
Split-dose radiotherapy	34	11	32
Cautery excision and radon seeds with and without supplemental radical neck dissection	14	4	29
Total	116	35	30
Orthovoltage roentgen therapy	34	9	26
Cobalt 60 teletherapy	68	21	31
Tumor-dose range			
$<5,000$ r	27	5	19
$\geqq 5,000$ r	74	25	34
$>6,000$ r	35	13	37
$>7,000$ r	11	5	45

TABLE IX

TREATMENT SUPPLEMENTAL TO EXTERNAL RADIOTHERAPY

Treatment	Result			
	Success		Failure	
	Patients	Per Cent	Patients	Per Cent
Combined continuous and split-dose	31	—	71	—
No radon seeds or surgery anytime	13	42	28	39
Radon seeds before external radiotherapy	6	19	16	23
Radon seeds just after external radiotherapy	1 (14)	3 (45)	4 (30)	6 (43)
Radon seeds > 3 mo. after external radiotherapy	7	23	10	14
Simple excision or cautery before external radiotherapy	3	10	0	—
Radical surgery before external radiotherapy	5* (11)	16 (36)	14† (23)	20 (33)
Surgery after external radiotherapy	3‡	10	9§	13
Salvage external radiotherapy after definitive external radiotherapy to primary site	2	6	9	13

* 4 commando procedures (2 surgical failures), 1 radical neck dissection.
† 12 radical neck dissections, 1 excision of lymph nodes, 1 excision of lymph nodes and primary lesion.
‡ 2 radical neck dissections, 1 laryngectomy.
§ 5 radical neck dissections, 2 commando procedures, 1 excison of lymph nodes, 1 pharyngectomy.

of patient management, split-dose methods remain, in the opinion of one of us (P.W.S.), the preferred methods of treatment if the patient with head and neck cancer is to receive supervoltage radiotherapy.

Again, similar to the series of carcinoma of the nasopharynx and the tonsil, in the present series we could detect no significant improvement in the 5 year survival rate attributable to the introduction of supervoltage methods, the end results remaining essentially the same whether the patient was treated by orthovoltage or supervoltage methods.

For the first time in this triad of nasoorohypopharyngeal malignancies, dose dependency apparently played some part in improving the 5 year survival rates. In our previously reported nasopharyngeal and tonsillar series, we could detect no appreciable difference in survival rate between patients treated by high dose methods (5,000 r or more) and those treated with substandard doses (less than 5,000 r). In this series, however, an apparent dose dependency was noted: of 27 patients receiving less than 5,000 r, 19 per cent survived more than 5 years in contrast to the survival of 34 per cent of 74 patients receiving a tumor dose of 5,000 r or more. The apparent superiority of higher dose regimens continued to be reflected as one ascended into the still higher dose ranges: of 35 patients receiving a tumor dose in excess of 6,000 r, 37 per cent survived more than 5 years, and of 11 patients receiving more than 7,000 r, 45 per cent survived more than 5 years. Because of the number of cases involved, however, one cannot say that these differences are of statistical significance.

Thus, in attempting to assess the effectiveness of 3 major changes in treatment techniques innovated during 11 years, we must confess to some inconsistency in the results obtained and attributable to such changes. In representatively large series of nasopharyngeal cancers (142 cases) and of tonsillar cancers (131 cases), there was no apparent improvement in end results attributable either to a change to a higher dose regimen in the earlier years of the period or to the advent of cobalt 60 teletherapy methods. There was, however, an apparent increase in effectiveness incurred in the change to split-dose methods in 1958. Contrariwise, in the present series of 116 cases of cancer of the base of the tongue, we could detect no apparent improvement in end results that could be attributed either to a change to split-dose methods or to a change to supervoltage techniques. There was, however, an apparent dose-dependency effect, with increasing 5 year survival rates being associated with a higher tumor-dose regimen—a dose-dependency effect we did not observe in the nasopharyngeal and tonsillar series.

FREQUENCY OF SECOND UNRELATED CANCERS

Another finding in the present series of cancers was the relatively high frequency of second or multiple carcinomas associated with the primary lesion of the base of the tongue. This tendency to develop other, apparently unrelated, distant malignant tumors was not observed in the previous series of nasopharyngeal or tonsillar carcinomas. In the present series, 17 patients (15 per cent) had apparently unrelated distant second lesions sometime after definitive treatment of the primary cancer in the base of the tongue (Table x). Of the 17, 9 had subsequent adenocarcinomas: 4 of the colon, 3 of the stomach, and 1 each of the prostate and breast. Five subsequently had squamous cell carcinoma apparently unrelated to the lesion of the base of the tongue, but, of course, in this particular instance, one cannot always be sure that the second lesions did not, in fact, represent true metastasis. Squamous cell carcinomas subsequently found in the parenchyma of the lung were not included as instances of a true second carcinoma. However, 2 of these 5 squamous cell carcinomas which developed in the main-stem bronchi were thought to be true primary bronchogenic carcinomas; the three others were located

TABLE X

SECOND APPARENTLY UNRELATED CANCERS FOLLOWING THERAPY OF CANCER OF THE BASE OF THE TONGUE

Lesion	Patients
Adenocarcinoma	9
Colon	4
Stomach	3
Prostate	1
Breast	1
Squamous cell carcinoma	5
Bronchus	2
Esophagus	1
Skin	1
Bladder	1
Large cell bronchogenic carcinoma	1
Melanoma	1
Transitional cell carcinoma of bladder	1
Lymphoma (associated with adenocarcinoma of colon)	1*
Total	17 (15 per cent of series)

* Patient included also among those with adenocarcinoma of colon.

in the esophagus, skin, and bladder, respectively. There was also one additional large cell bronchogenic carcinoma thought to represent an unrelated second malignancy. There was, in addition, one disseminated melanoma, one transitional cell epithelioma of the bladder, and one combined adenocarcinoma of the sigmoid and generalized lymphoma. The apparently increased incidence of second cancers associated with malignancies arising in the base of the tongue can only be noted and not evaluated at this time.

TREATMENT COMPLICATIONS OR SEQUELAE

The incidence of radiation complications or sequelae was also higher in this series than in our previously reported nasopharyngeal and tonsillar series (Table XI). There were 2 cases of definite radiation myelitis and 1 of possible radiation myelitis.

The first patient, a 55 year old man with a T1 N2 (Stage IV) lesion, received a split-dose course of treatment in the following manner: 14 (1 month) 14 = tumor dose of 5,300 r, through opposing 14×17 cm. right and left lateral portals with a two-in-one loading, cobalt 60 teletherapy being given. Two years and 2 months after completion of therapy, typical radiation myelitis developed which, in 3 months, had progressed to a Brown-Sequard syndrome. The patient died 3 years after completion of therapy.

The second patient with definite radiation myelitis, a 66 year old woman, had a T2 No (Stage II) lesion. A midline tumor dose of 7,400 r in 24 treatment days was effected through opposing 6×9 cm. right and left lateral portals, cobalt 60 teletherapy being given. Symptoms of beginning radiation myelopathy started $3\frac{1}{2}$ years after treatment, but the outcome was not fatal. The patient is alive almost 11 years after completion of treatment, although with hemiparesis of the right arm and leg and with incontinence of the bowel and bladder.

The third patient, with possible radiation myelopathy, was a 74 year old man who had a T2 No (Stage II) lesion. He received a midline tumor dose of 6,200 r in 22 treatment days through opposing 5×6 cm. right and left lateral portals, cobalt 60 teletherapy being given. When seen approximately $5\frac{1}{2}$ years after completion of treatment, he had difficulty swallowing and signs of questionable bulbar palsy. Neurologic examination could not discriminate

TABLE XI

SERIOUS COMPLICATIONS OR SEQUELAE OF TREATMENT IN 116 CASES

Complication or Sequela	Cases
Radiation myelitis	3
Radionecrosis, larynx	2
Radionecrosis, pharynx	1
Fatal hemorrhage	2
After radiotherapy	1
After attempted surgical salvage of radiation failure	1
Postoperative death, pancreatitis	1
Total	9*

* 8 per cent of series (7 per cent attributable to radiotherapy).

between amyotrophic lateral sclerosis or early radiation myelopathy, although probably the latter was the actual condition. The patient died of apparently unrelated causes some 6 years after therapy.

In addition to the patients with radiation myelitis, 3 patients had what was thought to be radionecrosis of the hypopharyngeal structures—the larynx in 2 and the entire pharynx in 1. The 2 with radionecrosis of the larynx had received, by orthovoltage techniques, tumor doses of 6,000 r in 25 treatment days and 4,750 r in 17 treatment days. The patient with radionecrosis of the pharynx had received a tumor dose of 7,800 r in 19 treatment days (whether inadvertently or not could not be ascertained from the records) and this also was given by orthovoltage methods. In all 3 cases, attempts had been made to verify persistent or residual carcinoma, but in each instance biopsy showed only inflammatory necrotic tissue. While the third patient undoubtedly had true radionecrosis, there is some doubt about the diagnosis of radionecrosis following conventional doses in standard treatment times; hence, one cannot rule out entirely the possibility that persistent malignancy rather than true radionecrosis was the cause of death.

There were 2 cases of fatal end-of-treatment hemorrhage which may or may not have been entirely related to irradiation, but in which undoubtedly irradiation was contributory in some manner.

The first patient, a 66 year old woman, had a T3 N1 (Stage III) lesion. She was given split-dose therapy in the following manner: 12 (3 weeks) 14 = tumor dose of 5,350 r, cobalt 60 teletherapy being administered through opposing 12×12 cm. portals. Three months after completion of therapy, a commando *en bloc* excison of residual tumor in the base of the tongue and the hemimandible and a radical dissection of the neck on the involved side were performed for residual Grade 3 squamous cell carcinoma involving the right lateral pharyngeal wall. Three weeks after completion of operation the patient died of exsanguinating hemorrhage from the carotid artery.

The second patient with fatal hemorrhage, a 62 year old woman, had a T2 N2 (Stage IV) lesion. She received a midline tumor dose of 3,350 r in 14 treatment days by orthovoltage techniques, opposing 10×15 cm. right and left lateral portals being used. Prior to external radiation therapy, fifteen 1.0 mc radon seeds were inserted into the primary lesion and eight 1.0 mc seeds were inserted into a metastatic mass in the right midcervical region. On the last day of treatment the patient died of exsanguinating hemorrhage from the primary cancer.

Thus, 8 (7 per cent) of the 116 patients had serious sequelae directly or indirectly attributable to radiation techniques. In addition, a 70 year old man with a T2 N2 (Stage IV) lesion underwent radical dissection of the right side of the neck for metastatically involved upper and middle deep jugular lymph nodes with muscle invasion, and had an implantation of twelve 1.3 mc radon seeds into the lesion at the right base of the tongue. On the 17th postoperative day he developed postoperative pancreatitis and died. If this last operative death is included, the number of deaths in the series was 9 (8 per cent).

SUMMARY

Data on 116 patients with cancer of the base of the tongue treated in the years 1952 through 1962 have been reviewed. The male:female ratio was 3.8:1 and the 5 year survival rate was 27 per cent for males and 42 per cent for females. Although the figures suggest a preferentially better survival rate for females, no statistical significance could be attached to this finding because of the number involved. The patients were almost exclusively in the fifth, sixth, seventh, and eighth decades of life and the 5 year survival rates were remarkably similar for the various age groups.

Presenting symptoms usually entailed some element of pain or unpleasant sensation directly attributable to the primary lesion, interference with deglutition or other basic functions of the tongue, or metastatic lymphadenopathy in the neck. No one

presenting symptom seems to carry a more ominous prognostic significance than the others. Patients presenting with symptoms of short duration seemed to survive a little longer than did those with symptoms of longer duration, but again the differences were not statistically significant.

Seventy-eight per cent of the patients had squamous cell carcinoma with a 5 year survival rate of 26 per cent, 11 per cent had lymphoma of varying types with a 5 year survival rate of 39 per cent and 11 per cent had miscellaneous, rare types of tumor. Patients with cancer apparently confined to the base of the tongue had a 5 year survival rate of 48 per cent, while regional dissemination naturally reduced the rate according to the extent of dissemination. Extension to the lateral hypopharyngeal wall apparently caused little reduction in 5 year survival rate, while dissemination in almost any other direction caused considerable reduction. Seventy per cent of the patients on admission had evidence of metastatic cervical lymphadenopathy and, of these, 24 per cent survived 5 years; when this was confined to the ipsilateral side of the neck, 28 per cent survived 5 years in contrast to 10 per cent of those with contralateral or bilateral metastatic lymphadenopathy. The cure rate decreased with the advancing stage of the disease, classified according to the T-N-M system: the 5 year survival rate was 56 per cent for patients with Stage I involvement, 50 per cent for Stage II, 28 per cent for Stage III, and 18 per cent for Stage IV. Of the 116 patients, 30 per cent survived more than 5 years.

Broad treatment categories consisted of: (1) 68 patients given continuous conventional radiotherapy with a 5 year survival rate of 29 per cent; (2) 34 patients treated by split-dose methods with a 5 year survival rate of 32 per cent; and (3) 14 patients treated by miscellaneous methods such as cautery excision and implantation of radon seeds with or without supplemental radical lymph node dis section, with a 5 year survival rate of 29 per cent. No improvement in treatment effectiveness could be ascertained from either a change to supervoltage or cobalt 60 methods in 1954 or a change to split-dose methods in 1958. An apparent dose-dependency, however, was noted: patients receiving suboptimal dose levels (below 5,000 r) had a 5 year survival rate of 19 per cent in contrast to 34 per cent with dose levels above this amount. An apparently increased incidence of second unrelated cancers appearing after treatment of the cancer of the base of the tongue was noted, 15 per cent of the series developing such additional neoplasms.

Seven per cent of the series had fatal complications following radiotherapy; these included radiation myelitis, local fatal radionecrosis, and exsanguinating post-treatment hemorrhage.

Paul W. Scanlon, M.D.
Section of Therapeutic Radiology
Mayo Clinic
Rochester, Minnesota 55901

Vol. 105, No. 1

TWENTY YEARS' EXPERIENCE WITH RADIATION THERAPY OF MEDULLOBLASTOMA*

By BERNARD S. ARON, M.D., D.M.R.T.
BROOKLYN, NEW YORK

MEDULLOBLASTOMA is a highly malignant brain tumor which arises predominantly in the posterior fossa and spreads into other areas of the central nervous system. It is frequent in children (18–35 per cent of all brain tumors in children[2,6]) but rare in adults. Radiation therapy plays a major role in treatment, as 5 year survivals of 20 per cent,[2] 26 per cent,[7] 28 per cent,[6] and 41 per cent[5] have been reported after radiation therapy, while after surgery alone[1] there are almost no survivors.

Twenty-four patients with medulloblastoma were seen at the Kings County Hospital Center from 1946 to 1966; the diagnosis was made by the neuropathology department in all cases. No patients were lost to follow-up in this series.

CLINICAL DATA

The age and sex distribution may be seen in Figure 1 for the entire series and in Figure 2 for the patients who received radiation therapy. There were 17 children ranging in age from 4 months to 15 years; 3 children were under 1 year of age; the others were equally distributed from 1 to 15 years. There were 7 adults, ranging in age from 17 to 83 years; 4 adults were in the age range between 16 and 30 years.

A predominance of male to female ratio was found in this series, both in children (10 males to 7 females) and in adults (5 males to 2 females). In the total series there were 15 males to 9 females.

The most frequent presenting symptoms, both in children and adults, were headache, vomiting and ataxia. The average length of time of symptoms in children was 4 months, and the range was 2 weeks to 18 months.

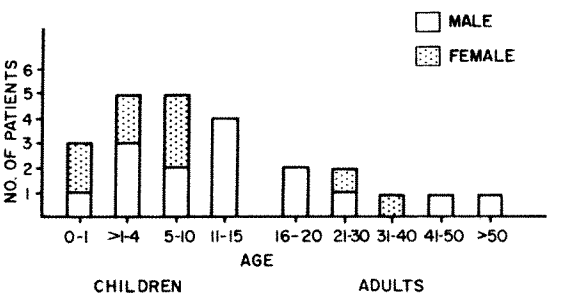


FIG. 1. Age and sex distribution of entire series.

The location of the tumor, either at the time of initial surgery or postmortem examination in patients who did not have surgery was predominantly in the posterior fossa. In children, all 17 patients had tumors of the posterior fossa. The lesions were located in the lateral cerebellar hemispheres in 3 patients and in the vermis in 6 patients. There was diffuse involvement in 4 patients and extension to the 4th ventricle in 5 patients. Meningeal seeding was present in 3 patients. In adults the tumor was in the posterior fossa in 6 patients (vermis, lateral cerebellar hemispheres or pons) and in 1 patient (age 83 years) in the left frontal lobe.

TREATMENT

There are 3 major treatment groups; (1) 3 patients had no treatment; (2) 21 patients had posterior fossa craniotomies; and (3) 15 of these patients had postoperative radiation therapy.

(1) The 3 patients who had no treatment (Table 1) were at the extremes of age distribution (4 months, 10 months and 83 years). One child (Case 20) presented in opisthotonus and died 2 days after admission. The other child (Case 22) presented as a hydrocephalic; he died 1 month after ad-

* From the Department of Radiology, Division of Radiotherapy, State University of New York, Downstate Medical Center and Kings County Hospital Center, Brooklyn, New York.

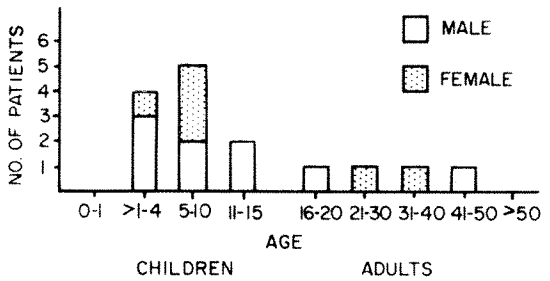


FIG. 2. Age and sex distribution of radiation therapy series.

mission. The adult (Case 19) had a history of epilepsy but came to the hospital after a fall and lapsed into coma with uremia (blood urea nitrogen 112 mg. per cent) and died 3 weeks after admission. Only the first patient (Case 20) was clinically suspected of having a brain tumor. The length of symptoms in these 3 patients was 4 months, 5 months and 1 day (fall before admission).

(2) There were 21 patients who underwent posterior fossa craniotomy; 4 died in the immediate postoperative period (within 1 day), resulting in an operative mortality of 19 per cent. Two patients subsequently died, 3 and 4 weeks postoperatively, before radiation therapy could be instituted. One patient (Case 8) had a shunt performed; he did well for 11 months, then there was clinical evidence of tumor recurrence, and he received radiation therapy. These patients are summarized in Table II.

(3) Fifteen patients received radiation therapy after posterior fossa exploration. No patients were treated without operation. Radiation therapy was usually begun 2 to 4 weeks after operation, and the patients frequently showed rapid clinical improvement during therapy. Details of radiation therapy will be discussed in a later section of this article. Nine patients showed recurrence of tumor after radiation therapy; all have died. All the children who died developed local recurrence, 6 out of 7, from 3 to 14 months (average 10 months) after treatment. One adult (Case 16) developed a local recurrence 2 years and 8 months and the other adult (Case 13) developed a metastasis to the fifth lumbar vertebral body 7 months after treatment. Two patients were re-treated (Cases 2 and 16); both died, at 6 months and 15 months after the second course of treatment. One boy (Case 11) developed convulsions 2 years and 6 months after treatment. For the next 3 years, his condition became progressively worse, with right hemiparesis, aphasia and finally death in status epilepticus, 5 years and 6 months after treatment. No postmortem examination was performed, and the clinical impression during his hospitalizations was "postradiation neuropathy." No lumbar puncture, arteriography or ventriculography was performed after radiation therapy. The diagnosis of "postradiation neuropathy" was

TABLE I

PATIENTS NOT TREATED

Case No.	Age	Sex	History	Survival Time from First Symptom until Death	Location of Tumor at Postmortem Examination
19	83 yr.	M	Epilepsy for many years; fall one day prior to admission	Three weeks after fall	Left frontal lobe
20	10 mo.	F	Vomiting for 5 months; lethargy; coma; opisthotonus	Five months	Cerebellum, extending into aqueduct of Sylvius
22	4 mo.	M	Excessive sleeping; slow growth rate	Five months	Right cerebellar hemisphere, extending to pons, medulla with leptomeningeal seeding

TABLE II

PATIENTS WHO DIED AFTER SURGERY

Case No.	Age (yr.)	Sex	History	Tumor Location (operative findings)	Survival Post Operation
12	12	M	No information	Meningeal seeding	One month
14	20	M	Ataxia, vomiting for 3 weeks	Pons shunt	Three weeks
15	29	M	Ataxia, headache, vertigo for 6 weeks	Left cerebellar hemisphere	One day
21	22 mo.	F	Ataxia, headache, vomiting for 2 months	Vermis into 4th ventricle	One day
23	5 mo.	F	Vomiting since birth	Right cerebellar hemisphere	One day
24	11	M	Vomiting, ataxia, headache for 6 months	Both cerebellar hemispheres to 4th ventricle	One day

TABLE III

PATIENTS WHO DIED AFTER RADIATION THERAPY

Case No.	Age (yr.)	Sex	History	Tumor Location	Recurrence		Survival Time
					Time	Location	
1	5	M	Headache, vomiting for 2 weeks	Left cerebellum	3 mo.	Local	10 mo.
2	10	F	Paresis, vomiting, headache	Cerebellum	2 yr. 3 mo.	Local	3 yr. 2 mo.
3	9½	F	Headache for 6 months	Posterior fossa	14 mo.	Local	18 mo.
7	2½	M	Vomiting, ataxia for 2 months	Vermis	7 mo.	Local	7 mo. (11 mo. postoperative)
8	15	M	Ataxia, eye signs for 7 months	Vermis, brain stem	4 mo.	Local	15 mo.
9	4½	M	No information	Cerebellum	10 mo.	Local	14 mo.
10	2½	M	No information	Cerebellar tonsils	6 mo.	Local	10 mo.
11	13	M	Headache, vomiting, double vision for 10 days	Vermis, 4th ventricle	2 yr. 6 mo.	Brain	5 yr. 6 mo. (post radiation effect)
13	17	M	No information	Vermis	7 mo.	L5 vertebra	12 mo.
16	35	F	Headache	Vermis	2 yr. 8 mo.	Local	4 yr. 2 mo. (2nd radiation therapy)

TABLE IV

PATIENTS ALIVE AFTER RADIATION THERAPY

Case No.	Age (yr.)	Sex	History	Tumor Location	Clinical Status	Survival Time
4	6	F	Ataxia, tremors	Cerebellum to 4th ventricle	Hypothyroid	20 yr. 7 mo.
5	10	M	Ataxia	Left cerebellum, local seeding	Borderline mental defective	10 yr. 9 mo.
6	4	F	Ataxia	Vermis to 4th ventricle	Well	14 mo.
17	29	F	Headache, vomitive ataxia	Vermis for 2 years	Spastic gait for 2 years then well	8 yr. 7 mo.
18	42	M	Headache, decreased vision	Left cerebellar hemisphere	Well, works as waiter	18 mo.

probably correct in view of the 3 year time interval from symptoms until death. These patients are summarized in Table III.

SURVIVAL

No patients are alive who had no treatment or only surgery. The average length of time of survival of patients who had no treatment did not differ from the average length of time of symptoms suggesting that patients with medulloblastoma will die quickly unless surgical decompression and radiation therapy are performed.

Five patients are living without evidence of disease, ranging in time from 14 months to over 20 years. These patients are summarized in Table IV. Three patients (Cases 4, 5 and 17) are available for long term follow-up. One boy, age 10 when treated (Case 5) is a borderline mental defective and is unemployable. He is of normal stature and his bone roentgenograms are normal. One girl, age 6 when treated (Case 4) had amenorrhea at age 17 (11 years post-treatment) and was found to be hypothyroid. On thyroid replacement therapy she has normal periods but has not married. She is of short stature, like her parents. Her mental status is slightly below normal and her bone roentgenograms are normal. The third patient, an adult (Case 17), had spastic gait for 2 years after treatment but is now well, and has given birth to a normal child.

Modified Life Table Survival Study on the patients treated with irradiation and surgery suggests a 5 year survival of 35 per cent and a 10 year survival of 26 per cent. Eleven children were treated, yielding a 5 year survival of 29 per cent. Four adults were treated, yielding a 5 year survival of 39 per cent.

RADIATION THERAPY TECHNIQUE

Most authors agree that these patients should be treated with a fractionated course of radiation therapy, to a dose of 2,700 r to 4,000 r over 4 to 6 weeks to the entire central nervous system,[1,2,3,4,5,6,7] via multiple fields or preferably by a single field.[4,5]

Various radiation therapy techniques were employed during the 20 year period covered in this study, including a large single posterior field as well as multiple fields and using both orthovoltage (200 kv. and 250 kv.) and megavoltage (Co^{60}) therapy units. We have attempted to analyze these various types of treatment in terms of dose time factors and field arrangement factors.

As far as dose time factors are concerned,

1 patient (Case 8) received grossly inadequate dose (800 r in air to each of 4 skull fields in 2 weeks, 200 kv. unit); his tumor locally recurred 4 months after treatment. All of the other patients received doses ranging from 2,500 r in 3 weeks to 4,000 r in 7 weeks. Nine patients received doses of 2,500 r to 3,000 r in 4 to 9 weeks; 3 of these patients are alive and the average survival time of those patients who died after this treatment was 27 months. Five patients received doses of 4,000 r or more in 4 to 6 weeks; 2 of these patients are alive and the average survival time of those patients who died after this treatment was 26 months. There appears to be no difference in results with these 2 dose regimens, as may be seen in Table v. However, 8 out of 9 tumor recurrences were local (in the cerebellum); perhaps higher doses (up to 4,000 r in 3 weeks or 4,500 r in 5 weeks) are needed to permanently control the local tumor in the cerebellum.

As far as field arrangement is concerned, there was a significant difference noted with different arrangements. All patients (except the previously mentioned Case 8) received radiation therapy to the skull and entire spinal cord, usually via multiple fields to the spinal cord (except Case 6 who was treated with a single spade shaped posterior field as described by Paterson and Farr[4]). There were different field arrangements to cover the skull. These were classified as adequate and inadequate; the results are summarized in Table vi.

Adequate arrangements include the following: 5 patients (Cases 4, 5, 9, 11 and 17) were treated with orthovoltage, 4 cross-firing 10×10 cm. to 10×15 cm. fields (anterior, posterior, right and left lateral) to cover the entire skull. Two patients (Cases 6 and 18) were treated with posterior fields, including the skull and cervical spinal cord, and anterior wedge Co^{60} teletherapy fields to achieve a homogeneous dose distribution. We consider that these 7 patients had an adequate distribution of radiation to the entire skull. Five out of these 7 patients are alive.

Inadequate arrangements include the following: 3 patients (Cases 1, 3 and 10) received radiation therapy to the cerebellum only, via 3 fields of 10×10 cm. (right and left lateral and posterior). Four patients (Cases 2, 7, 13 and 16) received radiation therapy via parallel opposed pair, 200 kv. to 250 kv., 10×15 cm. right and left lateral fields. A total of 7 patients received inadequate coverage of the skull or an inhomogeneous field distribution (250 kv., postoperative); none of these patients are alive.

Table V

DOSE TIME FACTORS IN RADIATION THERAPY

Dose	Time	No. of Patients	No. Alive	Average Survival of Dead Patients
1,000 r	2 wk.	1	0	4 mo.
2,500–3,000 r	4–9 wk.	9	3	27 mo.
4,000 r	4–6 wk.	5	2	26 mo.

Table VI

FIELD ARRANGEMENTS IN RADIATION THERAPY

Type	No. of Patients	No. Alive
Adequate	7	5
Inadequate	8	0

SUMMARY

1. Twenty-four patients with medulloblastoma were seen at the Kings County Hospital Center from 1946 to 1966. This tumor was more frequent in children (17 patients) than in adults (7 patients). The age range was 5 months to 83 years. There was a male predominance in the series (15 males to 9 females).

2. These tumors are usually located in the cerebellum (23 out of 24 cases) and the patients presented with cerebellar symptoms (usually ataxia), as well as symptoms

of increased intracranial pressure (headache and vomiting).

3. No patients survived who were untreated or treated by surgery alone. The survival for untreated children was 5 months; the average length of time of symptoms in all the children was 4 months.

4. Five out of 15 patients treated by radiation therapy and surgery are alive. When the tumor recurred after treatment, it was usually in the cerebellum. There was no difference in results with either fractionated doses of 2,500 r to 3,000 r in 4 to 9 weeks or doses of 4,000 r in 4 to 6 weeks. There was a significant difference in results in patients who had adequate treatment coverage of the skull (5 out of 7 alive) as against inadequate field arrangement (none out of 8 alive); 1 patient developed convulsions following radiation therapy and died 5 years and 6 months after treatment.

5. Modified life table study suggests a 5 year survival of 35 per cent and a 10 year survival of 26 per cent after radiation therapy.

Department of Radiology
State University of New York
Downstate Medical Center
450 Clarkson Avenue
Brooklyn, New York 11203

REFERENCES

1. Bailey, P., and Cushing, H. Medulloblastoma cerebelli: common type of midcerebellar glioma of childhood. *Arch. Neurol. & Psychiat.*, 1925, *14*, 192–224.
2. Bouchard, J., and Peirce, C. B. Radiation therapy in management of neoplasms of central nervous system, with special note in regard to children: twenty years' experience, 1939–1958. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1960, *84*, 610–628.
3. Lampe, I., and MacIntyre, R. S. Experiences in radiation therapy of medulloblastoma of cerebellum. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1954, *71*, 659–688.
4. Paterson, E., and Farr, R. F. Cerebellar medulloblastoma: treatment by irradiation of whole central nervous system. *Acta radiol.*, 1953, *39*, 323–336.
5. Pearson, D. Personal communication.
6. Smith, R. A., Lampe, I., and Kahn, E. A. Prognosis of medulloblastoma in children. *J. Neurosurg.*, 1961, *18*, 91–97.
7. Tice, G. M. Treatment and prognosis of medulloblastoma. *J.A.M.A.*, 1962, *182*, 629–631.

Vol. 105, No. 1

THE TREATMENT AND PROGNOSIS OF MEDULLOBLASTOMA IN CHILDREN*

A STUDY OF 82 VERIFIED CASES

By H. J. G. BLOOM, M.D., M.R.C.P., F.F.R., E. N. K. WALLACE, M.B., D.M.R.T., *and* J. M. HENK, M.B., F.F.R.
LONDON, ENGLAND

IN 1925 Bailey and Cushing[2] identified the medulloblastoma as an entity, distinguishing it from the sarcomas and other posterior fossa gliomas. They described its natural history, and gave it the name by which it is known today. For nearly 50 years it has been appreciated that medulloblastomas are highly radiosensitive and that following postoperative irradiation, life is prolonged to a greater extent than after surgery alone. Coupled with this knowledge, however, has been an almost universal pessimism concerning the ultimate outcome. Most authors, even in recent years, regard the diagnosis of medulloblastoma as tantamount to a death sentence, with a life expectancy generally measured in months.

It is the purpose of this paper to report on early and late results of treatment in children under 15 years of age with cerebellar medulloblastoma, to evaluate factors influencing prognosis, and to consider the quality of life in long-term survivors. We hope to show that not only can a proportion of children with this tumor be cured by postoperative cerebrospinal axis irradiation, but that cure, in the majority of such cases, can be accomplished without serious radiation sequelae.

ETIOLOGY

During the development of the cerebellum, proliferation of neuroepithelial cells occurs in the posterior tip of the roof of the fourth ventricle to form the germinal bud: from here, undifferentiated cells migrate over the outer surface of the cerebellum as the external granular layer. Persistent foci of these primitive cells may be found in the region of the posterior medullary velum in children and even in adults.[43] It is postulated that under certain conditions in the fetus or later in life, these cells may undergo proliferation to form a medulloblastoma. The stimulus could be provided by a neurotropic virus or chemical carcinogen, both of which can pass the placental and blood-brain barriers in the fetus. Druckery *et al.*,[22] for example, have recently reported that a single injection of ethylnitrosourea to pregnant rats resulted in tumors of the nervous system in the offspring, but not in the mothers.

Medulloblastoma constitutes approximately 4 per cent of all tumors of the central nervous system (Table I), and some 20 per cent of intracranial neoplasms in children (Table II). In practice it is a rare tumor, and we have estimated that in England and Wales there are only about 60 new cases per annum.*

PREVIOUS SERIES

Following a vast surgical effort in 61 cases, and with a case mortality of 32 per cent, Cushing[17] was left with only 1 patient alive at 3 years. Half his cases received limited postoperative irradiation. It soon became clear that radical surgery alone was not enough to control medulloblastoma; that irradiation of the whole ventricular

* This figure is based on the reported annual incidence of cases of brain tumor in children 0–14 years of age supplied by 4 national cancer registration regions (population 0–14 years = 10.7 million) in England and Wales. From these statistics we estimated that there are rather less than 300 new brain tumor cases per annum in the country as a whole, of which some 20 per cent are medulloblastomas (*i.e.*, 60 cases).

* Presented at the Forty-ninth Annual Meeting of the American Radium Society, Toronto, Ontario, Canada, May 29–31, 1967.
From the Royal Marsden Hospital and Institute of Cancer Research, London, S.W.3, England.

TABLE I

INCIDENCE OF MEDULLOBLASTOMA IN ALL INTRACRANIAL TUMORS

Author	Total Cases	Medulloblastomas	
		No.	Per Cent
Cushing (1932)	2,023	86	4.3
Zülch (1965)	6,000	230	3.8
Berger and Elvidge (1963)	2,443	109	4.5
Total	10,466	425	4.1

system and spinal cord was necessary to prolong life appreciably, and that better results followed higher doses given in a single course. In spite of these observations, very few long-term survivors were subsequently reported, such cases being regarded as rarities.[28,41]

Lampe and MacIntyre[30] searched the literature between 1925 and 1948 and were only able to find a total of 27 3 year survivors, of which 12 were alive 3 to 9 years after treatment. These authors had 21 personal cases under 15 years of age, 6 of whom (28 per cent) were alive more than 3 years after treatment.

TABLE II

INCIDENCE OF MEDULLOBLASTOMAS IN CHILDHOOD INTRACRANIAL TUMORS

Author	Age Group	Total Intracranial Tumors	Medulloblastomas	
			No.	Per Cent
Cushing (1927)	Preadolescent	154	24	16
Zülch (1937)	<20	120	23	19
Bailey *et al.* (1939)	≤15	100	19	19
Craig *et al.* (1949)	<15	427	86	20
Bodian and Lawson (1953)	<13	129	25	19

After Crue (1958).

In the 1950s, very poor survival rates for medulloblastoma continued to appear in the literature, although two encouraging reports concerning a small number of cases were published in England in 1953. Paterson and Farr[39] were able to claim 7 of 13 children, and Richmond[46] 7 of 14 alive 3 years after treatment. During the past decade 5 year survival rates beyond all previous expectations have been reported from England by Paterson[37] (41 per cent of 27 cases), from the United States by Smith *et al.*[52] (28 per cent of 38 cases), and from Canada by Bouchard[8] (27 per cent of 37 cases). These results must be compared to the hopeless background of a life expectancy of 8 or 9 months from the clinical onset for untreated cases.[17] In reports concerning radiotherapy for medulloblastoma, the number of cases has usually been small and details of possible case selection have often been incomplete.

ROYAL MARSDEN HOSPITAL SERIES

Between 1950 and 1964, 108 cases of histologically verified medulloblastoma were referred to the Radiotherapy Department of the Royal Marsden Hospital (Table III). Of these, 3 were located in the supratentorial region, 2 had been previously treated, and 5, for domestic reasons, were referred for treatment to centers nearer their home. A further 16 cases were older than 15 years. After excluding these 26 cases, there remained for evaluation 82 children under the age of 15 years with medulloblastoma of the cerebellum.

TABLE III

ROYAL MARSDEN HOSPITAL MEDULLOBLASTOMA 1950–1964

Total Cases Referred		108
Supratentorial	3	26
Treated Previously	2	
Referred Elsewhere	5	
Adults (≥15)	16	
Cerebellar Medulloblastoma in Children (<15)		82

The diagnosis in all 82 cases has been based on histologic material seen by 2 or 3 pathologists at London Teaching Hospitals. Dr. N. F. C. Gowing (Director, Department of Morbid Anatomy, Royal Marsden Hospital) was able to obtain the histologic sections of 72 of the 82 cases for further review; the diagnosis in all 72 was confirmed once again.

Cerebellar medulloblastoma constitutes approximately one-third of all intracranial tumors in patients under the age of 15 years referred for irradiation to this hospital. Brain tumors in children occur with equal frequency in boys and girls. The medulloblastoma, however, is twice as common in males (Table IV). Eighty per cent of all medulloblastomas occur under the age of 15 years. The age distribution in the present series (Fig. 1) was comparable to that in 400 cases collected from the literature by Crue.[16] Our youngest child was 11 months of age. Two minor peaks can be seen around the ages of 3 to 4 years, and 8 to 9 years.

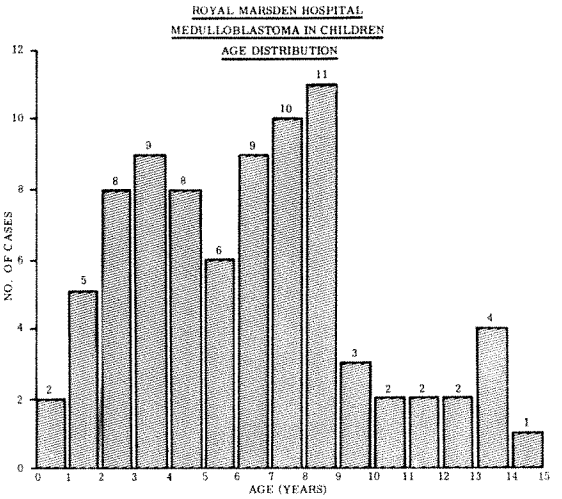


FIG. 1.

TECHNIQUES OF RADIOTHERAPY

There is now general agreement that the entire cerebrospinal axis must be irradiated in cases of medulloblastoma. We have not, however, adhered to the principle of uniform dosage throughout the treated volume, which has been the practice in some centers. We believe that it is essential to concentrate on the primary site and the region of immediate direct tumor extension, since in practically all of the children that we have failed to cure, there has been evidence of persistent or recurrent tumor in the cerebellum and brain stem region. In 14 cases subjected to autopsy in the present series, 13 were found to have tumor at, or in the vicinity of, the original primary growth. For this reason, the maximum dose is directed to the infratentorial region and to the third ventricle. We aim to complete treatment to the head before starting on the spine because of the risk of leukopenia, which may cause irradiation to be suspended.

TABLE IV

ROYAL MARSDEN HOSPITAL
INTRACRANIAL TUMORS IN CHILDREN <15 REFERRED TO RADIOTHERAPY DEPARTMENT
(1950–1964)

	Cases	Males	Females	♂ : ♀ Ratio
Medulloblastoma	82	56	26	2.2:1
Other Intracranial Tumors	178	91	87	1:1

At the Royal Marsden Hospital prior to 1959 several radiotherapy techniques were employed for medulloblastoma. All but 2 of the cases had cerebrospinal axis irradiation, but in most patients part of the brain, the frontal poles and, in some, the vertex, were outside the planned treated volume. There was much variation in dosage but the cerebellum and the upper cervical cord, in continuity with the brain-stem, generally received a tumor dose of 4,000–5,500 r in 5–8 weeks from 250 kv. roentgen rays (half value layer, 3.4 mm. Cu). The spinal skin dose was usually 3,000 r in 6–8 weeks. This resulted in a tissue dose of approximately 1,900 r (phantom measurements) to the remaining part of the cord. The full dose range varied between 1,000 and 3,900 r to the spinal skin, and between 2,000 to 6,700 r at depth in the posterior cranial fossa.

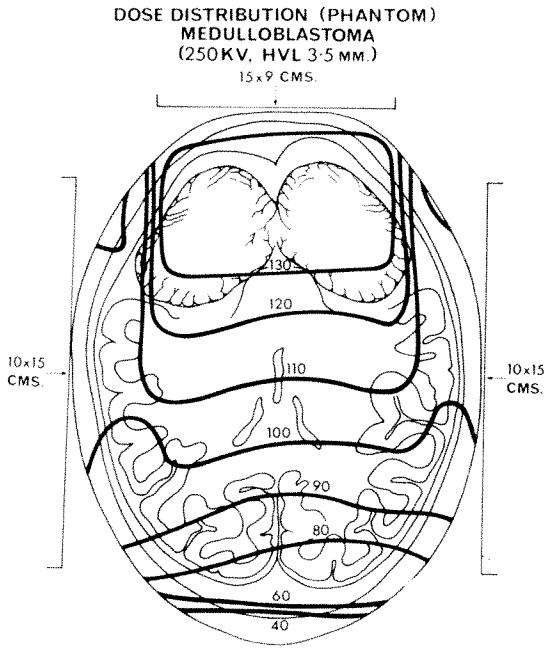


FIG. 2.

Since 1959, a more uniform technique has been employed, the purpose of which has been to treat the entire intracranial cavity and spinal theca. The skull was irradiated

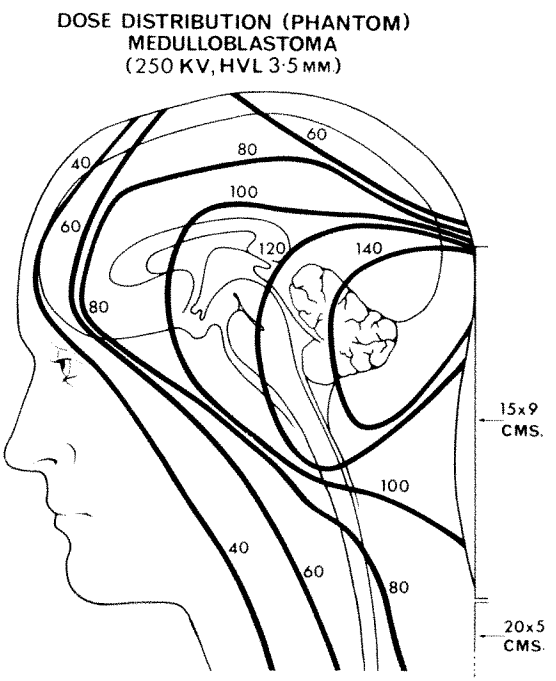


FIG. 3.

with a posterior and two opposing lateral fields (Fig. 2 and 3). The posterior fossa generally received a maximum dose of 4,500–5,000 r in 6–7 weeks; the dose to the mid-portion of the brain was 3,500–4,000 r, and to the frontal poles 2,500–3,000 r. The skin dose over the spine was 3,000 r in 5–6 weeks using contiguous fields of unequal length which were changed around after every 1,000 r to avoid "hot" and "cold" areas at junction zones. With older children we are now using 6 mev. roentgen rays from a linear accelerator, the maximum dose to the brain being 5,000 rads. The spine is treated with a single field and the cord dose is 3,000 rads.

RESULTS

Radiotherapy results in medulloblastoma are necessarily based on selected cases, and the over-all picture regarding outcome in this disease will not emerge until an account is taken of the substantial operative mortality, (presently, approximately 20–25 per cent) and of the cases that die before irradiation is started or completed. Our results are based on operative survivors. Eight children (10 per cent) who were in very poor condition on admission for radiotherapy, and in whom treatment was not completed because of their further deterioration or early death, have *not* been excluded from the series.

During the first 2 years following treatment there is a rapid decline in survival, after which the "force of mortality" appears to decrease. At 3 years, 35 per cent of 77 children are alive; at 5 years 32 per cent of 68 cases; and at 10 years 26 per cent of 34 cases (Table v).

CASES COMPLETING TREATMENT

Five of the 82 children in the present series died during treatment, and in 6 irradiation was abandoned—in 3 because of deterioration, in 1 at the request of the parents, and in 2 because of some doubt regarding the diagnosis which, however, was subsequently confirmed at autopsy. These 11 cases may be excluded to show the re-

sults in 71 patients who completed the prescribed treatment. Practically 40 per cent of such cases survived 5 years, and 30 per cent 10 years (Table VI; Fig. 4).

FACTORS INFLUENCING PROGNOSIS

AGE

It is generally believed that the prognosis in medulloblastoma is more favorable for teen-agers and adults than for young children. Sixteen adult cases treated at the Royal Marsden Hospital appeared to fare better than the children during the first 5 years after treatment; the ultimate prognosis, however, is more promising for children, in whom there is a 10 year survival rate of 26 per cent (Fig. 5).

The results for children by age group are shown in Table VII and Figure 6. Most deaths are seen to occur during the first 2 or 3 years following treatment. The steepest part of the declining survival curve is reached at 1 year for the children under 5 years, at 2 years for those aged 5–9 years, and at 3 years for the oldest group, 10–14 years. By this time the proportion alive in all 3 age groups is practically identical. *Compared with adults, the tempo of the disease is faster in children, and the younger the patient the quicker will unsuccessful cases die.*

TABLE V

ROYAL MARSDEN HOSPITAL, 1950–1964
MEDULLOBLASTOMA IN CHILDREN (<15)

Interval (yr.)	Cases	Alive	
		No.	Per Cent
2	82	37	45
3	77	27	35
5	68	22	32
7	58	13	22
10	34	9	26

TABLE VI

ROYAL MARSDEN HOSPITAL
MEDULLOBLASTOMA IN CHILDREN (1950–1964)
SURVIVAL IN PATIENTS COMPLETING TREATMENT

Interval (yr.)	Cases	Alive	
		No.	Per Cent
3	66	26	39
5	58	22	38
10	29	9	31

SEX

The possible influence of sex on prognosis does not appear to have received attention from previous authors other than Paterson,[37] who remarked that "treatment is more successful in girls than in boys." In the present series the outlook was appreciably better for girls, as judged by the 3, 5 and 10 year survival results (Table VIII).

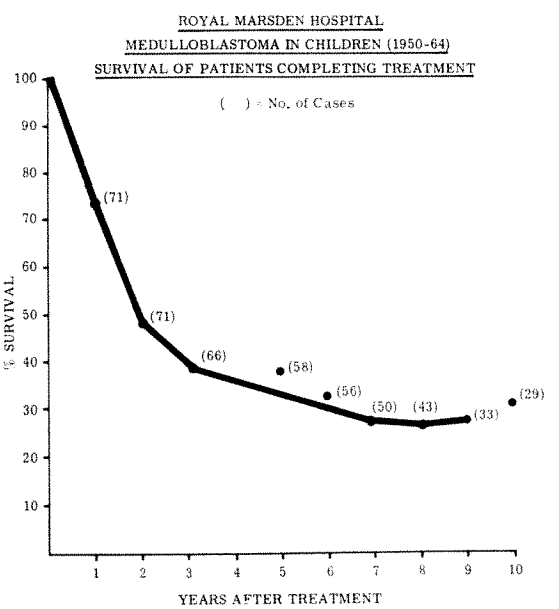


FIG. 4.

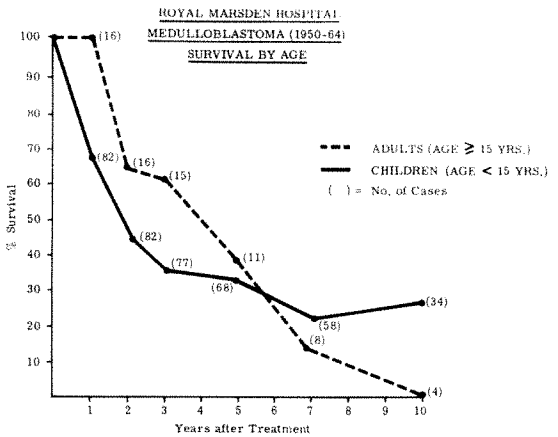


FIG. 5.

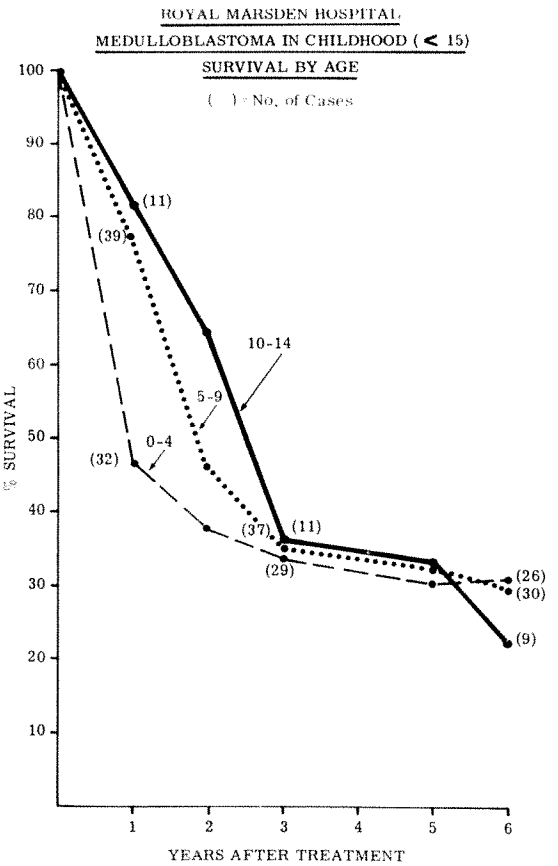


FIG. 6.

EXTENT OF DISEASE

It was possible to assess the presence or absence of brain-stem involvement from the surgical notes in 77 of the 82 patients. Radiotherapy appears to control even locally advanced disease for a considerable time, the influence of brain-stem invasion and probably other lines of local extension becoming evident only after the passage of more than 5 years (Table IX). Ultimately, only 2 of 12 cases with spread to the floor of the fourth ventricle were alive at 10 years, compared with 7 of 18 children in whom this complication was not present.

DELAY IN TREATMENT

No consistent correlation between prognosis and duration of symptoms could be demonstrated in the present series. The mean delay for 45 cases dying within 2 years of treatment was 3.2 months, compared with 3.6 months for 22 cases surviving 5 years, and 2.8 months for 9 cases

TABLE VII

ROYAL MARSDEN HOSPITAL
MEDULLOBLASTOMA IN CHILDREN
SURVIVAL BY AGE

Interval (yr.)	Age 0–4 years			Age 5–9 years			Age 10–14 years		
	Cases	Alive		Cases	Alive		Cases	Alive	
		No.	Per Cent		No.	Per Cent		No.	Per Cent
1	32	15	47	39	30	77	11	9	82
2	32	12	38	39	18	46	11	7	64
3	29	10	34	37	13	35	11	4	36
5	26	8	31	33	11	33	9	3	33

alive at 10 years. On the other hand, in patients with more advanced disease, as judged by the presence of brain-stem involvement at operation, there was a mean delay of 4.7 months, compared with 3.0 months for those without this complication.

HISTOLOGIC TYPE AND GRADE OF TUMOR

The so-called "cerebellar arachnoid sarcoma" is regarded by many pathologists as being merely a desmoplastic variant of the classical medulloblastoma, and this is supported by the finding of transitional forms between the two types.[20,49] The term "desmoplastic medulloblastoma" has been suggested for this variant because of the conspicuous connective tissue elements present which are ascribed to a marked leptomeningeal reaction secondary to tumor invasion. There appears to be little difference in the natural history of both types of tumor and treatment is the same. Nevertheless, they should be distinguished, as far as results are concerned, because of the somewhat better prognosis claimed for the desmoplastic variety in older children and adults. Dr. Gowing considered that only 3 of the 72 cases he reviewed in the present series could be classified as distinct examples of this type of tumor, but because of the small number involved we have not separated them from the main series. All 3 cases died within a year of treatment.

Unsuccessful efforts have been made in the past to correlate prognosis with histologic grade of malignancy in medulloblastoma.[19,50,53] Gowing has attempted to grade the cases in the present series according to degree of tumor differentiation, nuclear pleomorphism, frequency of mitoses and the amount of reticulin present, but no correlation could be demonstrated between any of these factors and survival.

Table VIII

ROYAL MARSDEN HOSPITAL
MEDULLOBLASTOMA IN CHILDREN
SURVIVAL BY SEX

Interval (yr.)	Boys		Girls	
	Cases	Alive (Per Cent)	Cases	Alive (Per Cent)
2	56	45	26	46
3	55	31	22	45
5	49	29	19	42
10	25	20	9	44

Table IX

ROYAL MARSDEN HOSPITAL
MEDULLOBLASTOMA IN CHILDREN
BRAIN STEM INVOLVEMENT AND PROGNOSIS

Interval (yr.)	Brain Stem*		Brain Stem†	
	Cases	Alive (Per Cent)	Cases	Alive (Per Cent)
3	44	36	27	37
5	39	36	25	32
7	33	30	22	14
10	18	39	12	17

*= Free.
†= Involved.

SURGERY AND TYPE OF OPERATION

Radical surgery alone cannot be expected to control medulloblastoma; without irradiation all patients with this tumor will die, usually within 6 months of operation. This was recognized by Cushing[17] who also stressed that the immediate surgical risk was greater than for any other intracranial tumor. His operative and case mortalities were 25 and 32 per cent, respectively. Even today, in the best hands, the mortality for radical surgery in children suffering from this tumor is not less than 20 per cent. To avoid the immediate loss of life due to operation, Cutler *et al.*[19] suggested that irradiation might be used without preliminary decompression. Peirce *et al.*[40] also recommended radiotherapy as the sole treatment, but advised preliminary closed aspiration biopsy to establish the diagnosis. Needle biopsy, however, is not without risk, since 3

TABLE X

ROYAL MARSDEN HOSPITAL
CHILDREN WITH MEDULLOBLASTOMA
REFERRED FOR RADIOTHERAPY
SURVIVAL BY TYPE OF OPERATION

Interval (yr.)	"Complete" Excision		Partial Excision	
	Cases	Alive (Per Cent)	Cases	Alive (Per Cent)
3	22	45	46	33
5	20	40	39	33
10	9	44	18	22

of 24 cases reported by Berger and Elvidge[4] died as a result of this procedure.

Elsberg and Gotten[23] showed that a conservative surgical approach (*i.e.*, decompression with removal of enough tumor for histology followed by radiotherapy) gave an average survival among the operation survivors comparable to that of a similar group of cases treated by radical surgery and irradiation; the operative mortality in the latter group, however, was 36 per cent, compared with only 13 per cent for the conservative surgical procedure. Most neurosurgeons today will attempt to remove as much of the tumor as possible without increasing unduly the operative mortality and risk of serious neurologic disability. Such a procedure will establish the diagnosis, create a decompression and reopen the cerebrospinal fluid pathway, which is the most certain way of preserving vision. In addition, by removing the bulk of tumor, including necrotic and anoxic elements, one hopes to assist in the task of destroying residual growth by irradiation.

In the present series a partial excision of the tumor was carried out in 50 children, and an apparently complete removal was effected in 23. Six children were submitted to biopsy only, and 3 were treated solely by irradiation, histologic verification in the latter cases being obtained subsequently at postmortem examination. The survival rate appears to be rather better following so-called complete excision of the tumor, but presumably this procedure is more likely to be accomplished in the more favorable cases (Table x).

RADIOTHERAPY TECHNIQUE

As stated previously, since 1959 a single irradiation technique has been used to include the whole intracranial cavity and spinal theca. A comparison of the results obtained before and after 1959 is shown in Table XI, with perhaps some improvement during the latter period.

The vast majority of fatal cases of medulloblastoma have persistent or recurrent disease at the primary site, and so a limited area of the cerebral hemispheres, which is not included in the treated volume, is unlikely to be responsible for an appreciable decline in survival, providing that the entire ventricular system and spinal theca are irradiated. In some cases, however, therapeutic failure can undoubtedly be ascribed to incomplete treatment of the central nervous system.

DOSE OF IRRADIATION

Arnold *et al.*[1] considered that tumors in the region of the brain-stem are incurable by irradiation because the necessary dose is likely to exceed the normal tolerance of this part of the brain. From our experience with

TABLE XI

ROYAL MARSDEN HOSPITAL
MEDULLOBLASTOMA IN CHILDREN
SURVIVAL OF CASES 1959–1964

Interval (yr.)	1950–1958		1959–1964*	
	Cases	Alive (Per Cent)	Cases	Alive (Per Cent)
2	50	38	32	53
3	50	30	27	44
5	50	30	18	39

* Cases treated by a more uniform technique. Whole central nervous system irradiation. Maximum dose (posterior fossa) 4,000–5,000 r.

TABLE XII

ROYAL MARSDEN HOSPITAL
MEDULLOBLASTOMA IN CHILDREN
SURVIVAL BY RADIATION DOSE

Dose*	2 Year Results		3 Year Results		5 Year Results	
	Cases	Alive (Per Cent)	Cases	Alive (Per Cent)	Cases	Alive (Per Cent)
<3,500 r	4	25	4	25	4	25
3,500–4,000 r	7	43	7	29	6	33
4,000–4,500 r	25	64	25	48	22	41
4,500–5,000 r	14	36	13	38	12	33
>5,000 r	22	45	18	33	18	33

* Maximum to posterior fossa.

older children and with adults, the brain-stem appears to tolerate a maximum dose of 5,000 rads in 6–7 weeks from telecobalt or supervoltage roentgen-ray equipment. In the present series a maximum tumor dose of less than 4,000 r with 250 kv. roentgen rays appears to be inadequate for the treatment of medulloblastoma in children, whereas a dose of 5,000 r or more *per se* might be excessive (Table XII).

CAN CHILDREN WITH MEDULLOBLASTOMA BE CURED?

The concept of a "period of risk" for recurrence of embryonal tumors is based on the assumption that the growth rate of individual tumors is constant and dependent upon age; the younger the child, the more rapid the tumor growth. If at the end of the period of risk, defined as the age at treatment plus 9 months for gestation, there is no clinical evidence of recurrence, then the prognosis is considered to be excellent.[14] This idea was first formulated for Wilms' tumor, and although exceptions have been reported, most cases appear to fit the rule.

Since medulloblastoma appears to be an embryonal tumor, we applied the concept of "age at treatment plus 9 months" as a possible test of cure in the present series (Fig. 7). The oblique line in this figure represents the end of the "period of risk." No deaths have taken place to the right of the line, except 1 due to intercurrent disease. So far, all recurrences in our series of 82 children with medulloblastoma have occurred within the period of risk as defined above. Once a child with medulloblastoma passes this critical period without signs of recurrence, cure seems likely.

RECURRENCE AND RETREATMENT

Although cerebrospinal metastases are often present in fatal cases of medulloblastoma, the chief cause of failure, in our experience, has been recurrence of the original primary tumor. Of 14 patients in whom an autopsy was performed, 13 had tumor in the posterior fossa; the remaining case died of meningitis shortly after treatment with no sign of residual neoplasm. Occasionally, distant metastases occur in medulloblastoma.[5,26,38,48] Two girls in the present series, both aged 8 years when treated, are known to have subsequently developed skeletal deposits; osteosclerotic changes were present in both cases, and in 1 the nature of the bone lesions was confirmed at postmortem examination.

Retreatment of children with distressing symptoms (*e.g.*, dysphagia, root pain) due to tumor recurrence following the initial

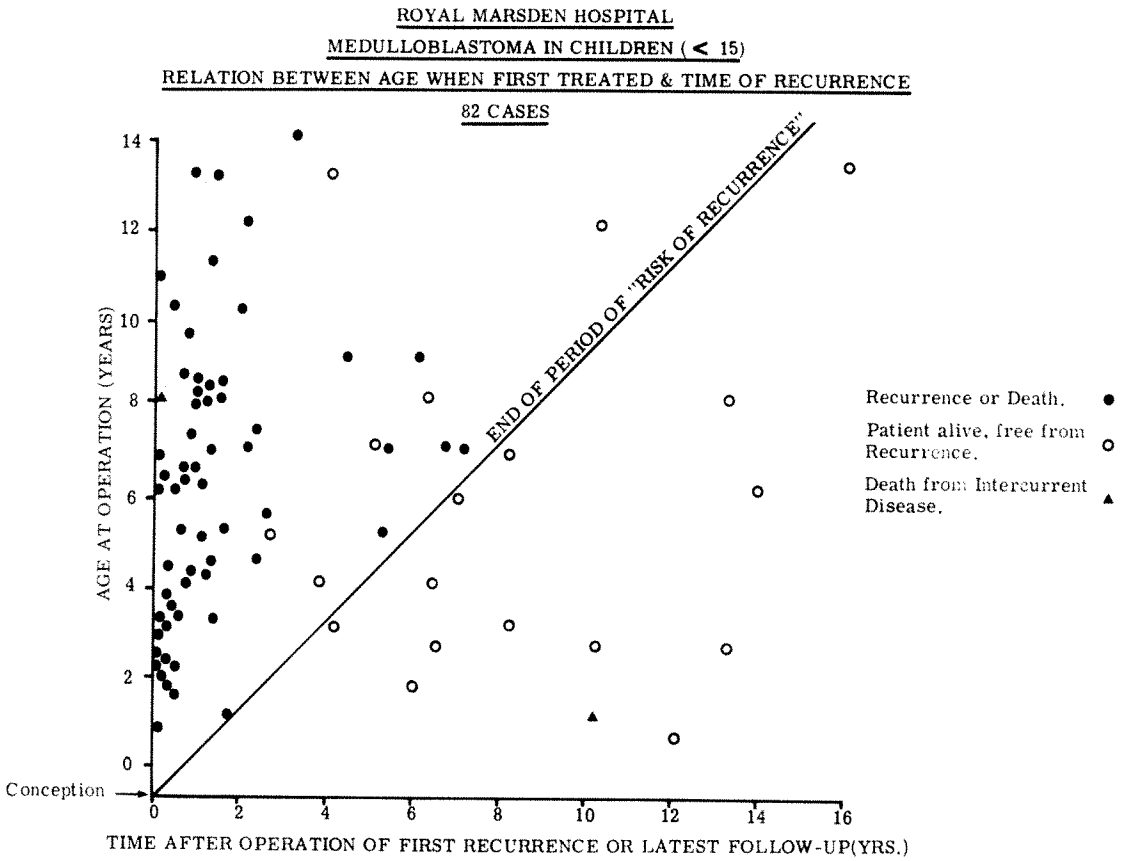


FIG. 7. All known recurrences of medulloblastoma have occurred to the left of the oblique line, *i.e.*, within the "period of risk" defined as age at treatment plus 9 months for gestation. Some patients, still well, have yet to pass the line.

radical course of radiotherapy is justified and often worthwhile. Irradiation in such cases should be limited to the affected areas and the dose restricted to that which brings relief (generally 1,500–2,000 r). An attempt at more radical treatment should be made for patients developing a recurrence in a previously untreated or low dose area. In the present series 16 courses of retreatment were given to 13 patients. Symptomatic relief was obtained on 9 occasions; 3 patients returned to active life for periods of from 13 months to over 3 years.

Remission in recurrent cases has also been reported following systemic chemotherapy with vincristine.[32] The subject of tumor recurrence in medulloblastoma and its treatment by irradiation and chemotherapy will be dealt with in greater detail in a separate communication.

QUALITY OF LIFE AND POSSIBLE LATE COMPLICATIONS IN MEDULLOBLASTOMA SURVIVORS

Lampe[29,31] has stressed that although some children with medulloblastoma appear to be cured, this may be at the price of serious brain damage due to irradiation. This complication was regarded as being present in 5, or perhaps 6, of 10 cases in his series surviving 5–15 years following a dose of 2,500 r in 7–10 days. Seven other patients in Lampe's series were treated by a more protracted technique, 5,000–6,000 r in 55 to 65 days, and of these, 4 were alive and well 3 to 6 years later, but 2 were said to be slow in learning.

The risk of radiotherapy for children with brain tumors may be considered from 2 aspects. First, gross brain damage or necrosis may occur, which is nearly always fa-

tal, and second, it is conceivable that more subtle neuropathologic changes may develop, producing an impaired intellect or disturbed emotions. One must also consider the consequences of irradiating extraneurologic structures such as the cranial bones, spine, marrow, pituitary, eye, and thyroid.

CENTRAL NERVOUS SYSTEM

(*a*) *Gross Damage* (*Necrosis*). In cases of medulloblastoma the brain-stem and upper cervical cord, which are considered to be among the most radiosensitive parts of the central nervous system, lie within the region receiving the maximum dose of irradiation. From a review of the general literature, especially the material reported by Boden[6,7] and by Lindgren,[33] it appears that a brain dose exceeding 5,500 r in approximately 4 weeks is dangerous. Individual idiosyncrasy, however, may occur, and at least 4 cases have been reported in which necrosis of the cervical cord, brain-stem or hypothalamus has followed doses of 4,500 r in 4–6 weeks—a dose normally well tolerated by these regions.[1,15,36]

A surgeon, when faced with a lesion threatening life, is prepared to accept an appreciable operative mortality, and for medulloblastoma this is at least 20 per cent. In the same way, the radiotherapist must be ready to face the risk of radiation complications when attempting curative treatment for a lethal disease, providing, of course, that the risk is not so great that the loss exceeds any gain. For cerebral gliomas in general we consider that a dose of 5,000 rads to a large volume from megavoltage equipment protracted over 6–7 weeks, in all but perhaps the youngest children, offers the greatest chance of cure while carrying the lowest risk of complications.

(*b*) *Functional Sequelae.* Although thousands of roentgens are required to produce recognizable histologic changes in the mature central nervous system, the brain, physiologically speaking, appears to be sensitive to doses of only a few roentgens, as evidenced by electroencephalographic changes, and the response of conditioned animals. We were reasonably confident that our dose-time schedule for medulloblastoma, 4,500–5,000 r to the posterior fossa in 6–7 weeks, carried only a small risk of necrosis. We were less certain about the possibility of more subtle neuropathologic sequelae occurring, especially in very young children, which might lead to serious functional changes in those who were to become long-term survivors.

Furthermore, the central nervous system of the developing mammal is particularly sensitive to irradiation, and from experiments in rodents the amount of damage inflicted is directly related to the dose, and inversely related to the age of the individual at the time of exposure. This applies to intra-uterine life, but there is a "carry-over" into at least the early postnatal period. Unfortunately, the experimental investigations have been confined to the immediate postnatal period, and we know of no comparable studies in rather older animals. Clemente *et al.*[13] showed that abnormal neurologic signs and neuropathologic changes in rats occurred more frequently and were more severe following head doses of 125–500 r when delivered within 3–4 days of birth, compared with irradiation after this time. Fifteen day old rats required a dose at least 4 times as great to produce the same changes as in 1–2 day old animals. The spinal cord is also far more sensitive to irradiation in the neonatal period, compared with 2–3 weeks after birth.[24]

In early childhood is there a stage when the brain is hypersensitive to irradiation, and if so, when does normal tolerance develop? No new nerve cells seem to appear after birth; mitoses of neurones are not evident after the seventh fetal month.[44] Although full maturation of the central nervous system, as judged by the degree of myelinization, may not be reached until puberty or even much later, this process is complete in most regions of the brain and cord by the end of the second year of postnatal life, generally by the first.[56] If there is a stage of unique radiosensitivity during

TABLE XIII

ROYAL MARSDEN HOSPITAL
MEDULLOBLASTOMA IN CHILDHOOD
5 YEAR SURVIVAL IN CASES AGED ≤3 YEARS

Age	Cases	5 Year Survival
Under 1 year	2	1
1–2 Years	4	1
2–3 Years	7	4
3 Years	7	1
Total	20	7 (35%)

postnatal development of the child's brain, then, judging from animal experiments, this is likely to be confined to the first year or two of life.

Information regarding neurologic sequelae following brain irradiation in very young children is difficult to obtain because of the almost impossible task of differentiating clinically between damage resulting from treatment, and that from the original tumor and its associated hydrocephalus. In the present series, of 6 children irradiated under 2 years of age, there were 2 long-term survivors, and both were demented, blind and epileptic. On the other hand, 4 out of 7 children treated at age 2 to 3 survived 5 years (Table XIII): 3 appeared normal both physically and mentally, while the fourth was ataxic and said to be slow at school, but otherwise well.

From the available data regarding human brain development, the radiosensitivity of the central nervous system in young experimental animals and the clinical experience in the present series, we now have arbitrarily chosen the age of 3 years (when the brain has reached 75 per cent of the adult weight and myelinization is well advanced) below which to prescribe a reduced maximum dose of 4,000–4,500 r in 6–7 weeks. Older children appear to tolerate brain irradiation well, and for them the full adult dose of 5,000 r in 7 weeks is given. In reaching this decision we have tried to balance the possible risks of treatment against the known high local recurrence rate and rapidly fatal course of so many medulloblastomas.

In spite of the potential dangers associated with irradiation of the young central nervous system, Bouchard and Peirce[9] were able to report that 86 per cent of 30 children with various brain tumors surviving 5—20 years after radical irradiation were leading an active life.

FUNCTIONAL RESULTS IN ROYAL MARSDEN SERIES

We have classified the survivors in the present series according to 4 categories of functional result:

I. *No disability, active life.* Patients in this group have no abnormal neurologic signs other than nystagmus. Children who are said to be slow at learning, but who, on general examination, are bright and appear intelligent, are included in this category.

II. *Mild disability, active life.* Here there may be ocular paresis, limited intention tremor and mild ataxia.

III. *Partial disability.* Patients may be severely ataxic or have seriously reduced vision, but all are capable of self-care. They may have definite impairment of intellect, but are capable of being taught a trade.

IV. *Total disability.* These cases are incapable of self-care.

Groups I and II, taken together, probably correspond to the category of "active life" proposed by Bouchard and Peirce.[9] Of the 22 children surviving 5–17 years in the present series, 18 (82 per cent) have led an active life, 15 without disability, and 3 with mild disability (Tables XIV and XV). Two patients were partly disabled, and 2 in category IV were demented and incapable of self-care. These last 2 children, who were still alive at 10 years, were treated at the age of 11 months and 15 months, respectively. Although it is

possible that severe neurologic disability including dementia and blindness may result from irradiating a young developing brain, such tragic sequelae are more likely to be due to cerebral damage produced by the original tumor and its associated hydrocephalus; in some cases surgical trauma and complications may also play a part. Enlargement of the head and gross neurologic disability were, in fact, already present in both of our demented cases at the time of the original admission for radiotherapy.

In children with severe disability such as decerebrate rigidity it may be humane to withhold treatment for fear of curing a demented and paralyzed child. On the other hand, limited palliative treatment is indicated to relieve distressing symptoms, even in hopeless cases if the child is alert and orientated. Should there be any doubt concerning the justification of treatment, a trial of irradiation may be undertaken, reviewing the situation at frequent intervals and only abandoning therapy in the absence of clear signs of improvement.

We have recently re-examined 12 of the 19 cases in this series who are still alive 3 to 17 years after treatment; 5 of the 7 remaining cases lived abroad. Reports on the patients who were unable to attend were obtained from parents or local doctors. Six of the 12 children of school age were making satisfactory progress, but one was blind (Table XVI). School progress in 2 was not known. Three were said to be slow at learning, had increased emotional reactions and were attending special schools. Problems of this type may be related more to missed schooling, parental anxiety and difficulties in the home rather than to brain damage *per se*; a history of husband-wife conflict, possibly aggravated by the child's illness, was found in 2 cases.

Seven cases are now adults (Table XVI) and 6 of them are in good health and capable of earning their own living (3 secretaries; 1 electrician; 1 telephonist; 1 instrument engineer). One woman, treated 17 years ago at the age of 13, has been a personal secretary to a solicitor and

TABLE XIV

ROYAL MARSDEN HOSPITAL
MEDULLOBLASTOMA IN CHILDREN
CLINICAL POST-TREATMENT GROUPS

Interval (yr.)	Cases Alive	I	II	III	IV
5	22	15	3	2	2
7	13	8	1	2	2
10	9	5	1	1	2

TABLE XV

ROYAL MARSDEN HOSPITAL
MEDULLOBLASTOMA: QUALITY OF LIFE IN 22 CHILDREN WHO SURVIVED 5–17 YEARS AFTER TREATMENT

Group	Group	Cases	
		No.	Per Cent
Active Life	I+II	18	82
Partial Disability	III	2	9
Total Disability	IV	2	9
Total		22	100

TABLE XVI

ROYAL MARSDEN HOSPITAL
MEDULLOBLASTOMA: CONDITION OF 19 PATIENTS STILL ALIVE 3–17 YEARS AFTER TREATMENT

Age	Cases	Clinical Condition
Still of School Age	12	1 Demented 3 Special schools. Slow learning or behavior problem 1 Good progress at school for blind 5 Well. Normal schooling—good progress 2 Well. School progress unknown
Now Adults	7	1 Well, but backward 6 Well, (3 secretaries; electrician; telephonist; instrument engineer)

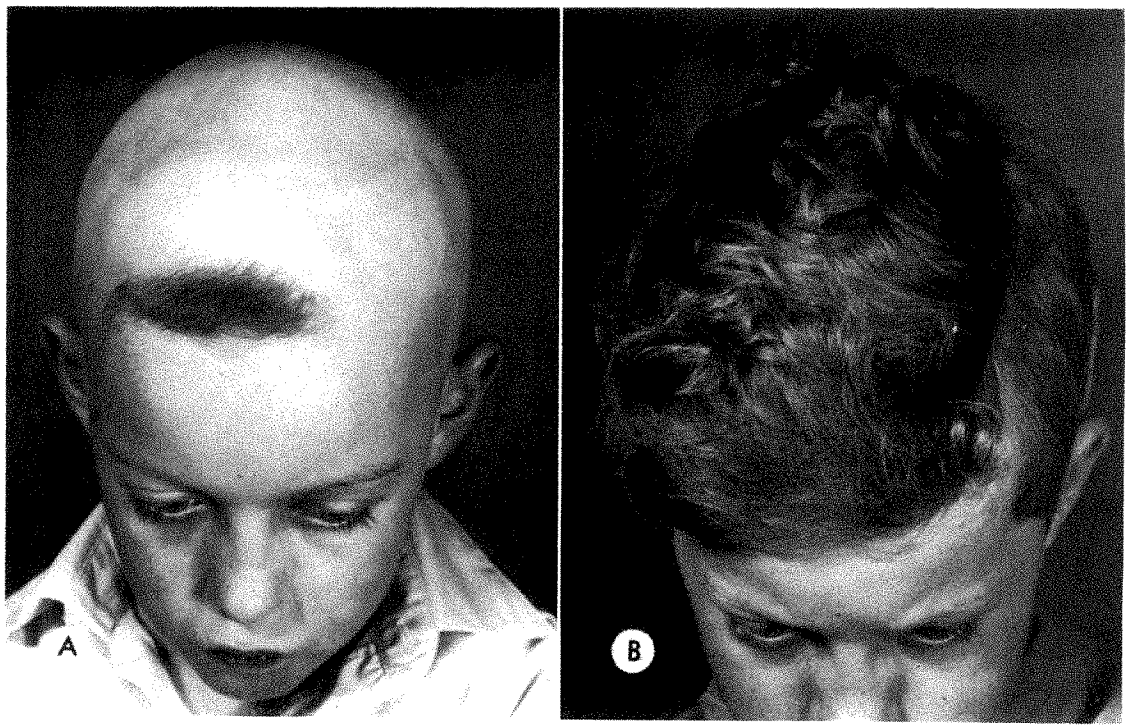


FIG. 8. (*A*) G. C., age 7. Total epilation, apart from small frontal tuft, following whole brain irradiation. (*B*) Full re-growth of wavy hair 8 months after treatment.

is now married with a normal child aged 2 years. The remaining case, a boy of 17, was treated at the age of 7 and is physically well, but mentally retarded: from the history and nature of the disability we believe this to be congenital and not acquired.

EXTRANEUROLOGIC TISSUES

(*a*) *Scalp and Skull.* Hair generally regrows well (Fig. 8, *A* and *B*), although some thinness and a bald patch or two may persist, especially in the occipital region at the site of the maximum dose of irradiation. A wig may be a great comfort to a sensitive girl or boy, but in most cases thin patches are well covered by hair from the surrounding regions of the scalp.

Berg *et al.*[3] have recently described 16 cases of osteonecrosis and 2 sarcomas of the cranium following irradiation for cerebral tumors. They reported that at least 7 of 35 cases of medulloblastoma (aged 3–18), and 6 of 55 cases of astrocytoma (aged 10–53) showed roentgenographic changes consistent with radiation necrosis. This condition appears to be symptomless and eventually becomes static or even regresses. In 1 of the 12 cases we have recently recalled for examination, 3–17 years after

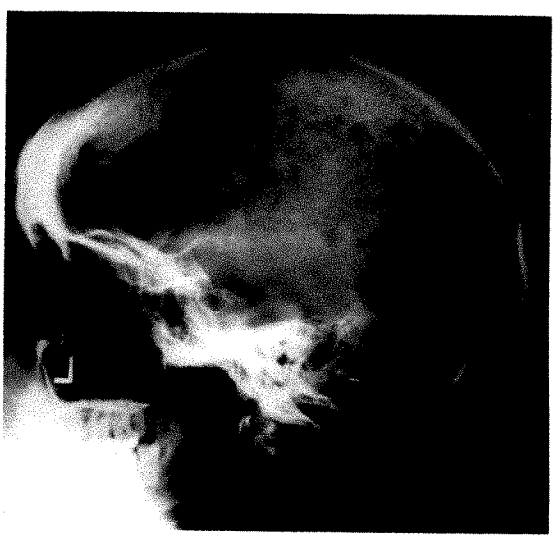


FIG. 9. L. W., roentgenogram of skull 15 years after treatment showing symptomless patchy osteoporosis probably secondary to irradiation.

treatment, the skull showed patchy osteoporosis of the parietal bones, the appearances being similar to those reported by Berg *et al.*[3] (Fig. 9). This female patient was 6 years old when treated, and is free from symptoms 15 years later.

(*b*) *Spine.* Neuhauser *et al.*[35] have reported that doses above 2,000 r of conventional roentgen irradiation (calculated at the center of the vertebral bodies) to the growing spine in children less than 2 years of age cause obvious roentgenologic changes. Rubin *et al.*[47] refer to 3 children aged 13 months to 5 years of age with medulloblastoma who each received a spinal cord dose of 3,000–3,200 r in 4 weeks with 280 kv. roentgen rays, and 1 other case, aged 4 years, who had 4,000 r in 4 weeks with 2 mev. equipment. In none of these cases were bone changes marked 2 to 7 years later.

In the present series the spine was clinically straight, and there were no obvious roentgenologic changes in any of the 12 cases recently re-examined 3–17 years after radiotherapy; their ages at the time of treatment had ranged between 2 and 13 years with 9 children less than 8 years. In some patients there may be reduction of stature but this is not marked. In our experience there appears to be little risk of producing serious disorders of bone growth following spinal irradiation (3,000 r skin dose) for medulloblastoma.

(*c*) *Eyes.* Britten *et al.*[11] have calculated that serious lens changes in adults (from radon seed implants) do not occur with doses of less than 2,000 r, but invariably follow 4,000 r or more. Qvist and Zachau-Christiansen[42] found that the minimum dose to produce cataract in children (from radium moulds) was 1,380 r; the maximum noncataract dose for infants was 990 r, and for children of school age, 1,140 r. On the other hand, Merriam and Focht[34] found that the lowest dose to the lens from fractionated roentgen therapy which produced cataract in children aged between 1 and 5 years was 650 r, and there was a 50 per cent incidence of opacities in lenses receiving between 530 and 1,050 r. Above 1,150 r, cataract occurred in all cases irrespective of age. Fortunately, the majority of cataracts occurring below a dose of 1,000 r seem to be stationary. The lenses of children under 1 year of age appear to be somewhat more sensitive to radiation than those of older children.[34]

Phantom and direct measurements have shown that the eye receives approximately 700 r from the 250 kv. technique used in our cases, which delivers a maximum tumor dose of 4,500–5,000 r to the posterior fossa in approximately 6 weeks. (With a more recent 6 mev. technique for older children we have been able to reduce the eye dose to 350 r.) No lens opacities were found in our limited material of 12 children recently examined by an ophthalmologist (Mr. J. M. Mallett) 3 to 17 years after treatment. In 27 children surviving at least 3 years, optic atrophy occurred in 5 cases, leading to impaired visual acuity in 2 and blindness in 3. This complication was undoubtedly secondary to raised intracranial pressure produced by the primary tumor.

(*d*) *Auditory Apparatus.* At this Hospital, Dias[21] has recently shown that following radical irradiation of the head and neck area there is generally no appreciable reduction in hearing as an early or late effect. In some cases slight impairment occurs, and this seems related to eustachian tube dysfunction, due either to the local effects of neighbouring tumor or to edema from radiation reaction. In the treatment of medulloblastoma, the auditory apparatus is included in the treated volume because of the necessity to extend the lateral skull fields inferiorly in order to cover the brain-stem fully. Hearing was normal in 11 of our 12 cases re-examined 3 to 17 years after treatment; a long-standing and probably unrelated unilateral labyrinthine disturbance was present in the remaining case.

(*e*) *Blood.* Some degree of leukopenia is the rule, but it is uncommon for treatment to be suspended for more than a few

days on account of a falling blood cell count. Occasionally, as the result of a serious reduction in count, the course of treatment may excessively prolonged and, rarely, may have to be abandoned altogether, short of the prescribed dose. Even in such cases, full recovery of the marrow generally occurs during the ensuing months. The blood cell count (hemoglobin, total and differential white blood cells and platelets) in the 12 recently re-examined cases surviving 3 to 17 years after treatment was normal.

(*f*) *Gonads.* The dose received by the ovaries from spinal irradiation with 250 kv. roentgen rays in little girls, based on phantom measurements, is approximately 120 r. No disturbance of menstrual function was observed in our cases; one of the girls subsequently married and has a normal child now aged 2 years. In boys the scrotal region receives between 40 and 75 r (direct measurement during treatment).

(*g*) *Sexual Development.* There was no evidence of endocrine dysfunction resulting from pituitary irradiation. In those patients who have reached adult life sexual development appears to be normal, while those who are still children appear to be developing satisfactorily.

(*h*) *Malignancy.*

(1) *Leukemia.* We know of no examples of leukemia and of aplastic anemia occurring in the present series, nor in those reported in the literature. This is not surprising, since radiation-induced leukemia in, for example, patients with ankylosing spondylitis is very low – an incidence of 4 per 1,000 cases being reported over a follow-up period averaging 13 years.[12]

(2) *Thyroid Carcinoma.* There is an increased risk of thyroid carcinoma when this gland has been irradiated in childhood or infancy, such as during the treatment of thymic enlargement. A substantial increase in the expected number of thyroid tumors occurs following doses of only 100 to 400 rads.[27] Raventos and Duszynski[45] reported 2 cases of thyroid carcinoma occurring 7 and 11 years after treatment for medulloblastoma in a boy aged $4\frac{1}{2}$ and a girl aged $7\frac{1}{2}$ years, respectively.

The dose to the thyroid of a child from a direct cervicodorsal spinal field during irradiation for medulloblastoma with 250 kv. roentgen rays is approximately 1,500 r. There were no known cases of thyroid tumor in our medulloblastoma series, but 1 of our patients, a boy aged 13 years, who received cerebrospinal irradiation for a fourth ventricle ependymoblastoma has developed a well-differentiated papillary thyroid carcinoma 6 years after radiotherapy. The estimated dose received by the thyroid from the spinal field was approximately 1,700 r. The tumor has been treated by hemithyroidectomy, and the patient is alive and well, 8 years after treatment for the brain tumor and 2 years after thyroid surgery. Fortunately, radiation-induced thyroid cancer generally responds well to surgical treatment.[27]

(3) *Bone Sarcoma.* This tumor following radiotherapy is extremely rare and is nearly always associated with gross radiation changes in the bone and overlying tissues—a feature not associated with the doses generally employed in the treatment of medulloblastoma.

(4) *Intracranial Tumors.* Radiation-induced intracranial tumors are extremely rare; they are usually fibrosarcomas and develop after a latent period of 5 to 20 years. Goldberg *et al.*[25] reported 4 instances of malignancy arising 10 to 30 years after irradiation in 75 cases of acromegaly. Waltz and Brownell[54] have recently reviewed the literature and refer to a case of medulloblastoma in whom a sarcoma of the tentorium developed 5 years after irradiation (with perhaps 3,500 r).

CONCLUSION

It is still a wide belief that medulloblastoma in childhood is inevitably fatal, and exceptions to this rule have been ascribed to errors in diagnosis,[57] or even to spontaneous regression.[10] All the 82 cases

in the present series have been histologically verified, and from the inevitably fatal outcome of inadequately treated cases in the past one can discount spontaneous regression as a factor responsible for long survival in this disease. The 5 and 10 year survival rates for patients completing the course of postoperative irradiation was 39 and 31 per cent, respectively.

Serious late changes in the central nervous system and extraneurologic tissues, consequent on cerebrospinal axis irradiation, appear to be rare with the dose-time factors recommended here; 18 of 22 cases surviving 5–17 years have led active lives. Slowness in learning and behavior problems, however, occur in some cases, and in occasional long-term survivors the neurologic disability is severe. When profound changes occur they are more likely to be the result of brain damage produced by the original tumor and associated hydrocephalus than by radiotherapy.

While the serious prognosis associated with medulloblastoma is fully justified, it appears that a totally pessimistic attitude is unwarranted. Parents can be given some hope for their stricken child who, if he survives his age at treatment plus 9 months, is likely to be cured.

SUMMARY

A study has been made of 82 histologically verified cases of medulloblastoma under 15 years of age referred for irradiation to the Royal Marsden Hospital between 1950 and 1964. The age range was 11 months to 14 years. The ratio of boys to girls was 2.2:1.

The tempo of the disease is faster in children than in adults and the younger the patient the more rapidly will unsuccessful cases die. Survival rates are greater for girls than for boys. In some cases with brain-stem involvement radiotherapy can cure or control locally advanced disease for an appreciable time. There is no correlation between outcome and histologic grade of tumor. The survival rate is greater for patients in whom a "complete" surgical excision of the tumor was performed, compared with lesser procedures.

Of 68 unselected cases followed for 5 years, 22 (32 per cent) have survived, and of 34 cases, 9 (26 per cent) are alive at 10 years.

The treatment advised for medulloblastoma is surgical exploration with removal of as much of the tumor as possible without increasing unduly the operative risk. This must be followed by irradiation of the entire cerebrospinal axis. At present, a maximum dose to the cerebellum and brain-stem of 4,000–4,500 r in 6–7 weeks is recommended for children under 3 years, and 4,500–5,000 r in 6–7 weeks for older children. The "prophylactic" dose to the remainder of the brain falls from 4,000 r in the middle region to 3,000 r at the frontal poles. The spinal cord receives 2,000–2,500 r. The cases reported here have been treated with 250 kv. roentgen rays. Megavoltage equipment (6 mev.) is now being used for older children.

Although widespread intrathecal tumor is generally present in fatal cases, the chief cause of therapeutic failure in medulloblastoma is persistence or recurrence of tumor at the primary site.

The survival rate increases with higher radiation doses to the posterior fossa, but there may be an optimum level above which results deteriorate; with orthovoltage roentgen rays this level may be approximately 4,500 r.

All recurrences in this series obeyed Collins' law for embryonal tumors and produced symptoms within a period of time corresponding to the patient's age at treatment plus 9 months for gestation. Once a child with medulloblastoma passes this critical period safely, cure seems likely. Limited retreatment of tumor recurrence by irradiation in previously radically irradiated cases is justified and often brings worthwhile relief of distressing symptoms.

In spite of the many potential late complications in the central nervous system

and extraneurologic tissues associated with cerebrospinal irradiation in young children with medulloblastoma, 18 of 22 patients (82 per cent) surviving 5 years had no serious disability and were leading active lives. Two children were partly disabled, and 2 others, treated at age 11 months and 15 months, respectively, were demented. Serious neurologic sequelae are more likely to be due to the original primary tumor and its associated hydrocephalus than to radiotherapy.

While the grave prognosis associated with medulloblastoma is fully justified, it appears that some hope can be given to parents of children with this disease, since practically 40 per cent of our cases completing treatment have survived 5 years, and 30 per cent, 10 years.

H. J. G. Bloom, M.D.
Radiotherapy Department
The Royal Marsden Hospital
Fulham Road
London, S.W.3
England

It is a pleasure to express our thanks to the neurosurgeons, especially Mr. Wylie McKissock and Mr. Kenneth Till, who have referred cases to us for radiotherapy, and with whom we have enjoyed a close and continued co-operation in the management of patients with tumors of the central nervous system. We are grateful to Professor D. W. Smithers for permission to include in this study cases prior to 1959, of which 10 were treated by Dr. S. Kramer.

We wish to thank Dr. N. F. C. Gowing for reviewing and grading the histologic sections, Mr. Peter Payne for information regarding the reported incidence of cerebral tumors in children in the South Metropolitan Cancer Region, Dr. B. Stedeford for help with phantom measurements, and the Departments of Medical Art and of Photography for the tables and illustrations.

REFERENCES

1. ARNOLD, A., BAILEY, P., and HARVEY, R. A. Intolerance of primate brainstem and hypothalamus to conventional and high energy radiation. *Neurology*, 1954, *4*, 575–585.
2. BAILEY, P., and CUSHING, H. Medulloblastoma cerebelli, common type of mid-cerebellar glioma of childhood. *Arch. Neurol. & Psychiat.*, 1925, *14*, 192–224.
3. BERG, N. O., LANDBERG, T., and LINDGREN, M. Osteonecrosis and sarcoma following irradiation of intracerebral tumours. *Acta radiol.*, 1966, *4*, 417–436.
4. BERGER, E. C., and ELVIDGE, A. R. Medulloblastoma and cerebellar sarcomas: clinical survey. *J. Neurosurg.*, 1963, *10*, 139–144.
5. BLACK, S. P., and KEATS, T. E. Generalized osteosclerosis secondary to metastatic medulloblastoma of cerebellum. *Radiology*, 1964, *82*, 395–400.
6. BODEN, G. Radiation myelitis of cervical spinal cord. *Brit. J. Radiol.*, 1948, *21*, 464–469.
7. BODEN, G. Radiation myelitis of brain stem. *J. Fac. Radiologists*, 1950, *1*, 79–94.
8. BOUCHARD, J. Radiation Therapy of Tumours and Diseases of the Nervous System. Henry Kimpton, London, 1966, pp. 104–118.
9. BOUCHARD, J., and PEIRCE, C. B. Radiation therapy in management of neoplasms of central nervous system, with special note in regard to children: twenty years experience, 1939–1958. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1960, *84*, 610–628.
10. BOYD, W. The Spontaneous Regression of Cancer. Charles C Thomas, Publisher, Springfield, Ill., 1966, p. 65.
11. BRITTEN, M. J., HALNAN, K. E., and MEREDITH, W. J. Radiation cataract: new evidence on radiation dosage to lens. *Brit. J. Radiol.*, 1966, *39*, 612–617.
12. BROWN, W. M., and DOLL, R. Mortality from cancer and other causes after radiotherapy for ankylosing spondylitis. *Brit. M. J.*, 1965, *2*, 1327–1332.
13. CLEMENTE, C. D., YAMAZAKI, J. N., BENNETT, L. R., and MCFALL, R. A. Brain radiation in newborn rats and differential effects of increased age. II. Microscopic observations. *Neurology*, 1960, *10*, 669–675.
14. COLLINS, V. P. Wilms' tumor: its behavior and prognosis. *J. Louisiana M. Soc.*, 1955, *107*, 474–480.
15. CROMPTON, M. R., and LAYTON, D. D. Delayed radionecrosis of brain following therapeutic x-radiation of pituitary. *Brain*, 1961, *84*, 85–101.
16. CRUE, B. L. Medulloblastoma. Charles C Thomas, Publisher, Springfield, Ill., 1958, p. 84.
17. CUSHING, H. Experiences with cerebellar medulloblastoma: critical review. *Acta path. et microbiol. scandinav.*, 1930, *7*, 1–86.
18. CUSHING, H. Intracranial Tumours. Charles C

Thomas, Publisher, Springfield, Ill., 1932, p. 150.

19. Cutler, E. C., Sosman, M. C., and Vaughan, W. W. Place of radiation in treatment of cerebellar medulloblastoma: report of 20 cases. Am. J. Roentgenol. & Rad. Therapy, 1936, *35*, 429–453.
20. Dexter, D., and Howell, D. A. Medulloblastomas and arachnoidal sarcomas. *Brain*, 1965, *88*, 367–374.
21. Dias, A. Effects on hearing of patients treated by irradiation in head and neck area. *J. Laryng. & Otol.*, 1966, *80*, 276–287.
22. Druckery, H., Ivanković, S., and Preussmann R. Teratogenic and carcinogenic effects in offspring after single injection of ethylnitrosourea to pregnant rats. *Nature*, 1966, *210*, 1378–1379.
23. Elsberg, C. A., and Gotten, N. Results of conservative compared with radical operations in cerebellar medulloblastomas. *Bull. Neurol. Inst. New York*, 1933–1934, *3*, 33–52.
24. Gilmore, S. A. Effects of x-irradiation on spinal cords of neonatal rats. I. Neurological observations. *J. Neuropath. & Exp. Neurol.*, 1963, *22*, 285–293.
25. Goldberg, M. B., Sheline, G. E., and Malamud, N. Malignant intracranial neoplasms, following radiation therapy for acromegaly. *Radiology*, 1963, *80*, 465–470.
26. Gyepes, M. T., and D'Angio, G. J. Extracranial metastases from central nervous system tumors in children and adolescents. *Radiology*, 1966, *87*, 55–63.
27. Hempelmann, L. H., Pifer, J. W., Burke, G. J., Terry, R., and Ames, W. R. Neoplasms in persons treated with x-rays in infancy for thymic enlargement: report of third follow-up survey. *J. Nat. Cancer Inst.*, 1967, *38*, 317–341.
28. Ingraham, F. D., and Bailey, O. T. Cerebellar medulloblastoma with verification nineteen years after onset of symptoms. *J. Neurosurg.*, 1944, *1*, 252–257.
29. Lampe, I. Radiation tolerance of central nervous system. In: Progress in Radiation Therapy. Edited by Buschke. Grune & Stratton, Inc., New York, 1958, pp. 224–236.
30. Lampe, I., and MacIntyre, R. S. Medulloblastoma of cerebellum. *Arch. Neurol. & Psychiat.*, 1949, *62*, 322–329.
31. Lampe, I., and MacIntyre, R. S. Experiences in radiation therapy of medulloblastoma of cerebellum. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1954, *71*, 659–668.
32. Lassman, L. P., Pearce, G. W., and Gang, J. Effect of vincristine sulphate on intracranial gliomata of childhood. *Brit. J. Surg.*, 1966, *53*, 774–777.
33. Lindgren, M. On tolerance of brain tissue and sensitivity of brain tumours to irradiation. *Acta radiol.*, 1958, Suppl. 170.
34. Merriam, G. R., Jr., and Focht, E. F. Clinical study of radiation cataracts and relationship to dose. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1957, *77*, 759–785.
35. Neuhauser, E. B. D., Wittenborg, M. H., Berman, C. Z., and Cohen, J. Irradiation effects of roentgen therapy on growing spine. *Radiology*, 1952, *59*, 637–650.
36. Pallis, C. A., Louis, S., and Morgan, R. L. Radiation myelopathy. *Brain*, 1961, *84*, 460–479.
37. Paterson, E. Malignant tumours of childhood. *J. Fac. Radiologists*, 1958, *9*, 170–174.
38. Paterson, E. Distant metastases from medulloblastoma of cerebellum. *Brain*, 1961, *84*, 301–309.
39. Paterson, E., and Farr, R. F. Cerebellar medulloblastoma: treatment of irradiation of whole central nervous system. *Acta radiol.*, 1953, *39*, 323–336.
40. Peirce, C. B., Cone, W. V., Bouchard, J., and Lewis, R. C. Medulloblastoma: non-operative management with roentgen therapy after aspiration biopsy. *Radiology*, 1949, *52*, 621–632.
41. Penfield, W., and Feindel, W. Medulloblastoma of cerebellum, with survival for seventeen years. *Arch. Neurol. & Psychiat.*, 1947, *57*, 481–484.
42. Qvist, C. F., and Zachau-Christiansen, B. Radiation cataract following fractionated radium therapy in childhood. *Acta radiol.*, 1959, *51*, 207–216.
43. Raaf, J., and Kernohan, J. W. Relation of abnormal collections of cells in posterior medullary velum of cerebellum to origin of medulloblastoma. *Arch. Neurol. & Psychiat.*, 1944, *52*, 163–169.
44. Rabinowicz, T. Discussion. Quantitative appraisal of the cerebral cortex of the premature infant of eight months. In: Regional Development of the Brain In Early Life. Edited by A. Minkowski. Blackwell Scientific Publications, Oxford, England, 1967, p. 124.
45. Raventos, A., and Duszynski, D. O. Thyroid cancer following irradiation for medulloblastoma. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1963, *89*, 175–181.
46. Richmond, J. J. Radiotherapy of intracranial tumors in children. *J. Fac. Radiologists*, 1953, *3*, 180–189.
47. Rubin, P., Duthie, R. B., and Young, L. W. Significance of scoliosis in post-irradiated Wilms' tumor and neuroblastoma. *Radiology*, 1962, *79*, 539–559.
48. Rubinstein, L. J. Extracranial metastases in cerebellar medulloblastoma. *J. Path. & Bact.*, 1959, *78*, 187–195.

49. RUBINSTEIN, L. J., and NORTHFIELD, D. W. Medulloblastoma and so-called "arachnoidal cerebellar sarcoma." *Brain*, 1964, *87*, 379–412.
50. RUSSELL, D. S., and RUBINSTEIN, L. J. Pathology of Tumours of the Nervous System. Edward Arnold & Co., London, 1959, p. 156.
51. SIMPSON, C. L., and HEMPELMANN, L. H. Association of tumors and roentgen-ray treatment of thorax in infancy. *Cancer*, 1957, *10*, 42–56.
52. SMITH, R. A., LAMPE, I., and KAHN, E. A. Prognosis of medulloblastoma in children. *J. Neurosurg.*, 1961, *18*, 91–97.
53. SPITZ, E. B., SHENKIN, H. A., and GRANT, F. C. Cerebellar medulloblastoma in adults. *Arch. Neurol & Psychiat.*, 1947, *57*, 417–422.
54. WALTZ, T. A., and BROWNELL, B. Sarcoma: possible late result of effective radiation therapy for pituitary adenoma: report of two cases. *J. Neurosurg.*, 1966, *24*, 901–907.
55. WILSON, G. M., KILPATRICK, R., ECKERT, H., CURRAN, R. C., JEPSON, R. P., BLOMFIELD, G. W., and MILLER, H. Thyroid neoplasms following irradiation. *Brit. M. J.*, 1959, *2*, 929–934.
56. YAKOVLEV, P. I., and LECOURS, A. R. In: Regional Development of the Brain in Early Life. Edited by A. Minkowski. Blackwell Scientific Publications, Oxford, England, 1967, pp. 3–64.
57. ZÜLCH, K. J. Brain Tumours. William Heinemann, Ltd., London, 1965, pp. 63, 133.

VOL. 105, NO. 1

ROENTGENOLOGIC CONSIDERATIONS OF THE HYOID APPARATUS

By SAAR PORRATH, M.D.
CANOGA PARK, CALIFORNIA

SPORADIC single case reports of hyoid bone fractures comprise the major share of the radiologic literature relating to this area. The term *hyoid apparatus* is inclusive for the hyoid bone, stylohyoid ligaments, styloid processes, and the hyoid-thyroid cartilage junction. The purpose of this paper is to present the regional anatomy, normal anatomic variants, and pathologic alterations which may occur.

In a 3 year period a total of 14 patients with abnormalities in this location were studied: 7 with anomalies and 7 with hyoid bone fractures.

NORMAL ROENTGEN ANATOMY

In man, the hyoid bone is U-shaped, lying in the anterior portion of the neck, between the symphysis of the mandible and the larynx. The bone consisting of a body and 2 paired processes, the lesser and greater cornua, is suspended from the styloid process of the temporal bone by the stylohyoid ligaments, which attach to the lesser cornua (Fig. 1, *A* and *B*).

STYLOID PROCESS

The styloid process is almost always present. It is normally cylindrical, broad based at the temporal bone and tapering toward a free extremity. It varies in length, thickness, form and shape.[24] Asymmetry may present in the same patient (Fig. 2, *A*, *B* and *C*). When an elongated styloid process projects against the tonsillar region of the soft palate it may cause a dull ache or pain usually radiating to the ear, commonly aggravated by swallowing.[5,7,8] An elongated styloid process is encountered about once in 3,000 tonsillectomies.[13]

Figure 3, *A* and *B* demonstrates an elongated right styloid process with a slight

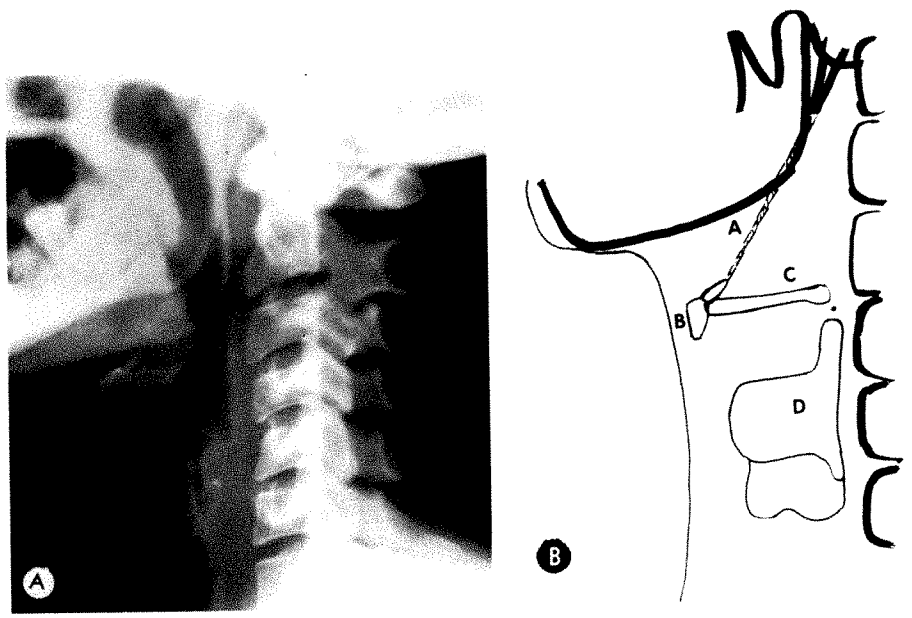


FIG. 1. (*A*) Normal hyoid bone. Note the relationship of the body of the hyoid to the greater cornua. (*B*) Line drawing of *A*. (A) The stylohyoid ligament, extending from the styloid process to the lesser cornu. (B) Body of hyoid bone. (C) Greater cornu. (D) Thyroid cartilage. Note small triticeous cartilage between cornu of hyoid bone and thyroid cartilage.

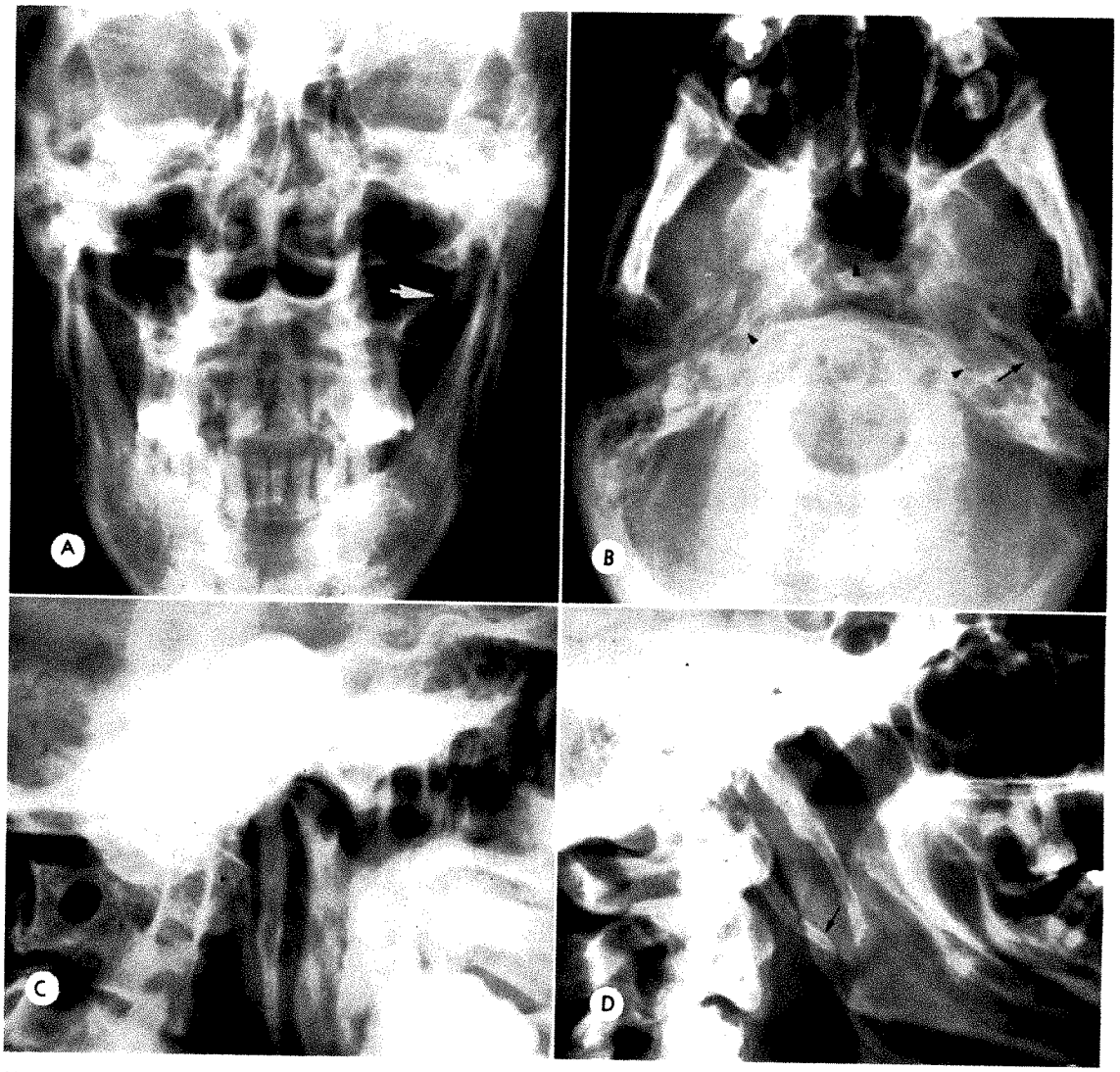


FIG. 2. (*A*) Posteroanterior roentgenogram showing asymmetry of the styloid processes. Note the curvature of the left process (arrow). (*B*) Inferosuperior projection (basal) of *A*. The arrow points to the curved left styloid process. The triangles outline the inner margin of the hyoid bone. The most anterior triangle shows the position of the body of the hyoid, the lateral triangles are at the posterior portions of the greater cornua. (*C*) Marked asymmetry of styloid processes. (*D*) Partial ossification of the stylohyoid ligaments. The arrow points to the unfused portion of ossification which should not be mistaken for a fracture.

inward curvature of the distal portion. The patient complained of pain radiating to the base of the tongue and the right side of the mandible. When the process was palpated intraorally the patient experienced similar pain. He refused surgical therapy.

THE STYLOHYOID LIGAMENT

The stylohyoid ligament, extending from the free tip of the styloid process to the lesser cornu, shows a great variation in degree of ossification, from none to complete (Fig. 4), as well as in length and width. Striking examples of ossification have been seen in children. Figure 5*A* shows the presence of bilateral ossification in a 2 year old boy and Figure 5*B* shows bilateral ossification, more marked, in an 8 year old girl. Fractures of the ossified ligament, if they occur at all, must be extremely rare; hence the partial unfused ossification

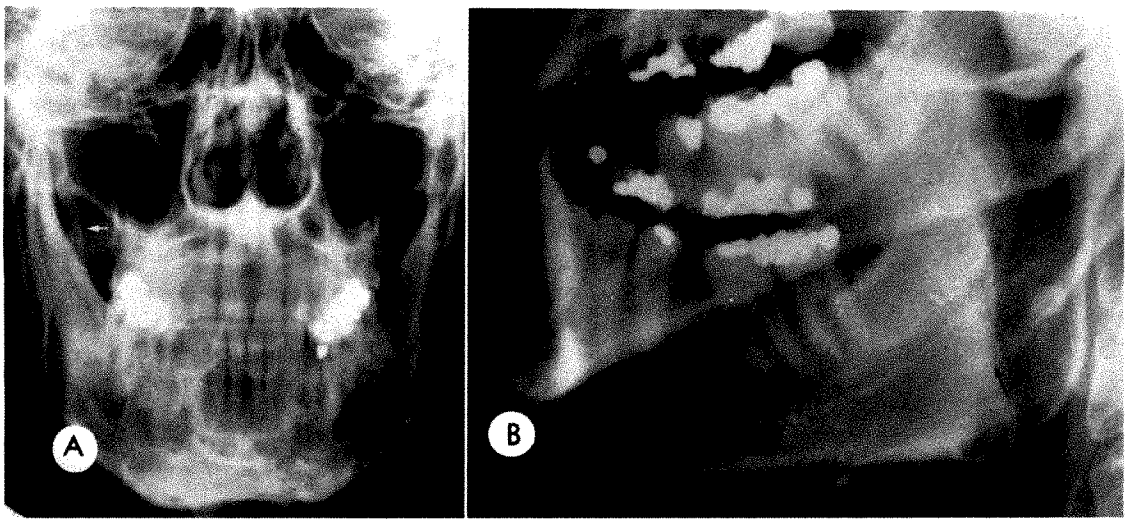


Fig. 3. (*A* and *B*) Elongated styloid process on the right (arrows). There is a slight inward curvature of the distal portion.

of the ligament must not be mistaken for a fracture (Fig. 2*D*).

LESSER CORNUA

The paired lesser cornua of the hyoid bone are typically small and conical shaped (Fig. 6). They are united to the body of the hyoid by fibrous tissue or a diarthroidal joint, which usually persists throughout life, but which may become ankylosed. Occasionally the lesser cornua also articulate with the greater cornua. The horns (cornua) usually appearing as small ossicles during the first and second years may persist into adult life as partially or completely cartilaginous.[1,2,11,17,24] They may appear elongated because of fusion with the distal ligamentous ossification. This should not be mistaken for duplication of the greater cornua.[17]

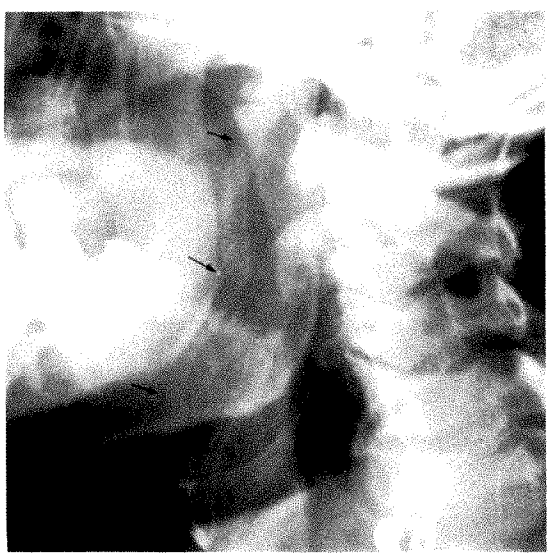


Fig. 4. Complete ossification of the stylohyoid ligament (arrows).

GREATER CORNUA

The paired greater cornua project upwards and backwards from the lateral borders of the body terminating posteriorly in tubercules, to which the lateral hyothyroid ligaments are attached. These ligaments extend between the greater cornua of the hyoid bone and the greater cornua of the thyroid cartilage. A small calcified triticeous cartilage is embedded in this ligament (Fig. 1*B*). The greater cornua seldom fuse with the body until the 35th to 45th years and occasionally remain ununited.[17]

HYOID BODY AND BURSA

The body of the hyoid is roughly quadrilateral, arranged transversely across the midline of the neck. The anterior surface is convex having many depressions where muscles attach. The posterior surface is smooth and concave, separated from the

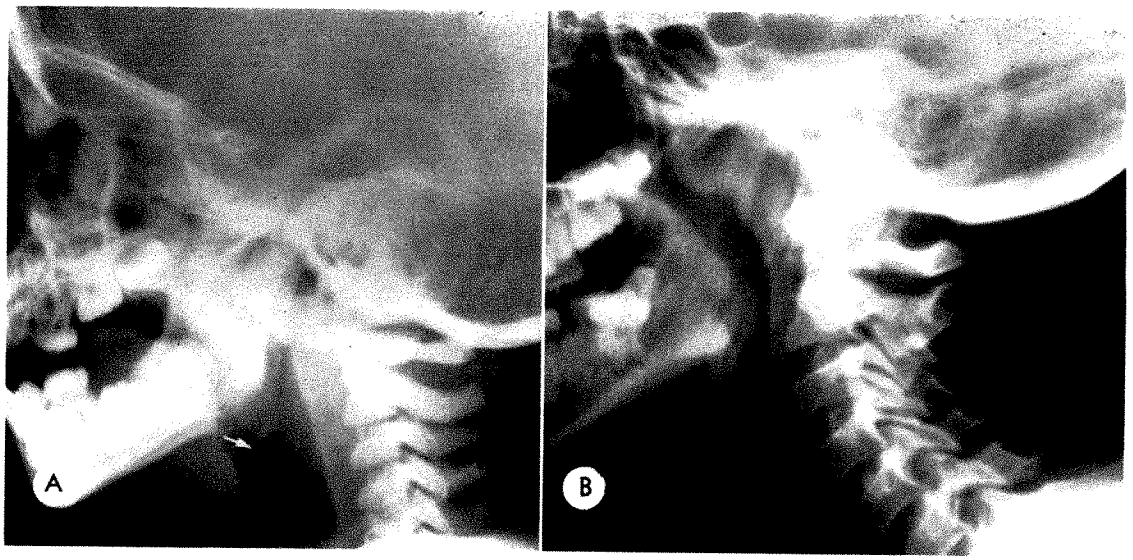


Fig. 5. (*A*) Bilateral partial ossification of the stylohyoid ligament in a 2 year old boy (arrow). (*B*) Bilateral partial ossification in an 8 year old girl.

epiglottis by the hyothyroid membrane and loose areolar tissue (note relationships in Fig. 1*A*). Interposed between the membrane and the bone is a synovial bursa which lessens the friction between the larynx and the hyoid during swallowing. Bursae as large as the distal portion of a thumb have been found. Nelson[14] in 1940 reported 31 cases of hyoid bursitis as a distinct clinical entity. It was 4 times more common in men than in women. Brown[3] in 1954 reported on the hyoid bone syndrome, differing only slightly from that of Nelson. Unfortunately, neither article reported roentgen findings.

EMBRYOLOGY

Embryologically, the second branchial arches become the styloid processes, stylohyoid ligaments, and lesser cornua of the hyoid bone. The ventral portions of the fourth branchial arches differentiate into the cuneiform and thyroid cartilages. Occasionally the fifth arches also contribute a portion of the thyroid cartilage.[1,2]

All told, there are 6 ossification centers; 2 for the lesser cornua, 2 for the greater cornua, and 2 for the body. Ossification of the body and greater cornua begins during the fifth prenatal months, so that the structures are visible at birth. Roentgenographically, they were seen in 60 and 59 per cent respectively of 1,000 normal newborn infants examined by Dedick and Caffey,[4] and in 75 per cent of 500 newborn infants examined by Tomstett and Donaldson.[25]

CONGENITAL HYOTHYROID BAR

Anomalies of the hyoid bone, and ossification of the hyothyroid ligaments, have been infrequently reported. It is probable

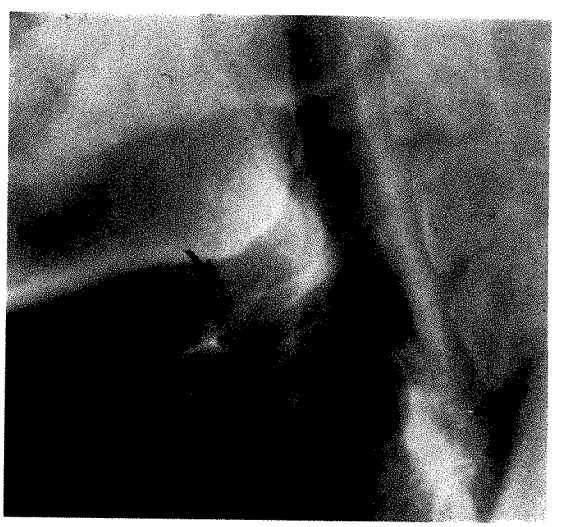


Fig. 6. Lesser cornua of the hyoid bone (arrow).

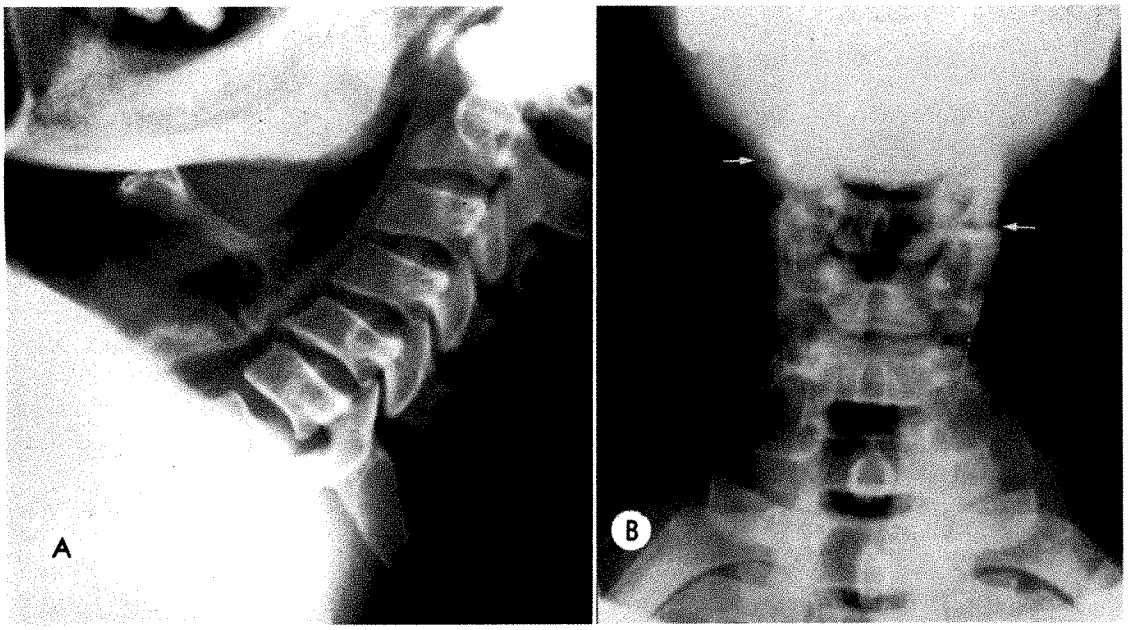


Fig. 7. (*A*) Bilateral ossification of the hyothyroid ligaments. Note union of process with hyoid bone on left and with thyroid cartilage on right. (*B*) Anteroposterior projection of *A*. Because of their size, the abnormal junctions can be seen in this projection (arrows).

that these are more common than suspected if only for the fact that they are not sought.

Seven patients were found to have an anomalous junction between the greater cornua of the hyoid bone and the greater cornua of the thyroid cartilage. All were examined roentgenographically for unrelated conditions. The 5 patients from whom a history was obtained denied prior trauma to the neck. They had neither limitation of motion nor dysphagia. In only 1 patient (no history could be obtained from this patient) was there a significant associated abnormality of the remainder of the hyoid apparatus and that was bilateral ossification of the stylohyoid ligaments.

Figure 7, *A* and *B* demonstrates bilateral ossification of the hyothyroid ligaments. On the left the ossification is united superiorly with the greater cornu of the hyoid body. Inferiorly the ligamentous attachment persists. On the right the ossification joins inferiorly with the greater cornu of the thyroid cartilage, the ligament persisting superiorly. Normally the hyoid bone is poorly visualized on the anteroposterior roentgenogram of the neck because of its superimposition on the vertebral column. Because of its size the anomalous junction may be seen in this projection (Fig. 7*B*).

Ossification may involve the central portion of the hyothyroid ligaments. There may be an associated enlargement of both the posterior portion of the greater cornua of the hyoid bone and the greater cornua of the thyroid cartilage. In addition the greater cornua of the hyoid bone are curved inferiorly. In Figure 8, the triticeous cartilage is incorporated into the central ossification. The ligamentous attachment remains superiorly and inferiorly. This is further demonstrated by a laminagram in the anteroposterior projection in another case (Fig. 9).

Figure 10 demonstrates a partial formation of the anomalous junction, present only on one side. The opposite side is normal. There is elongation and downward bending of the posterior portion of the greater cornu of the hyoid, without enlargement of the cornu of the thyroid cartilage or ossification of the ligament.



FIG. 8. Bilateral ossification of the hyothyroid ligaments. Note enlargement of the posterior portion of the greater cornua of the hyoid, and of the thyroid cartilage. The triticeous cartilage is incorporated into the central ossification.

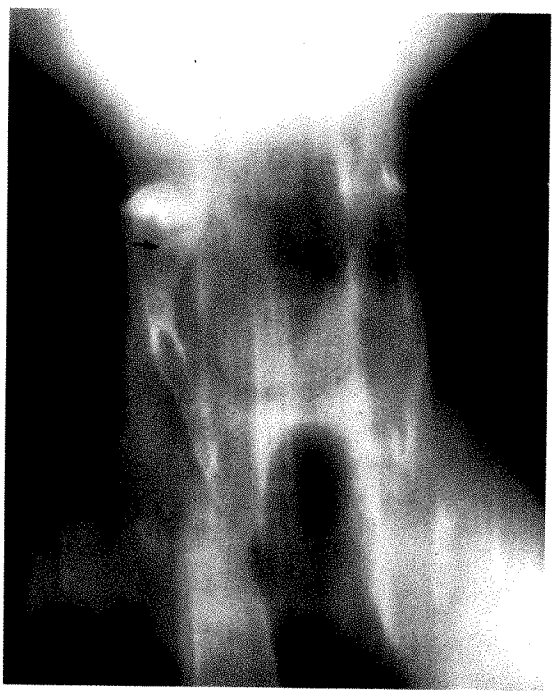


FIG. 9. Laminagram in the anteroposterior projection. The arrow points to the bar interposed between the hyoid and the thyroid cartilage. Note downward curvature of the greater cornu of the hyoid. Opposite side is out of focus.

Early in the embryologic development, the body of the hyoid and the laminae of the thyroid cartilage are joined by a curved cartilaginous bar, the hyothyroid cartilage. The cartilaginous bar remains until the third fetal month when it becomes discontinuous, being replaced by the hyothyroid ligament. Embedded in this ligament is a small cartilaginous island, the triticeous cartilage. During the process of formation of the triticeous cartilage, irregularities of segmentation of the fetal hyothyroid cartilage probably result in the accessory cartilages as well as the peculiar hyothyroid bars.[10]

The anomalous communication between the hyoid bone and the thyroid cartilage is an atavistic occurrence. In many mammals, the hyoid is of a different shape than in humans. The thyroid cornua of the hyoid in these animals correspond to the greater cornua of humans. In the dog communication between the greater cornu of the thyroid cartilage and thyroid cornu of the hyoid bone is of ligamentous tissue, formed by the lateral hyothyroid ligament as in man. In the horse and pig, in addition to this ligament there is a partial cartilaginous bar between the cornua (as in the human fetus). The ox and goat have a bony



FIG. 10. Unilateral partial ossification of the hyothyroid ligament. Note elongation and downward curve of the anomalous hyoid cornu.

junction present between the cornua with ossification of the ligaments.[9,16]

The lack of clinical symptomatology in current cases is in contradistinction to previous reports.[9,13] There was no limitation of motion or dysphagia. These symptoms have been recorded in patients with the elongated styloid process syndrome.[7] It is interesting to note that the previously reported cases of hyothyroid cartilage anomalies had an ossified stylohyoid chain. (Only 1 of the present 7 patients had ossification of the stylohyoid chain.)

There is no evidence that limitation of motion or dysphagia occurs in those animals with a partial or complete bony bar bridging the cornua. It is probable that when symptoms do arise, the patient has an associated abnormality, and that the anomalous junction of the hyoid bone and the thyroid cartilage is an incidental finding of no clinical significance.

No cases of duplication of either the greater cornua or lesser cornua were found in the literature. Sawwaf,[20] in unpublished material, found a congenital absence of the hyoid bone in a patient who came to autopsy. Silverman[22] has shown an example of "stippled epiphyses" of the hyoid bone.

The thyroglossal duct and cysts have a relationship to the hyoid embryologically. When seen, many of the ducts run through or directly behind the hyoid bone. Ward *et al.*[26] found a 25.6 per cent recurrence rate without hyoid removal in surgical treatment of thyroglossal ducts. Figure 11 shows the presence of a thyroglossal duct which has been injected with contrast material.



Fig. 11. Injected thyroglossal duct. Note extent towards tongue and relationship to the body of hyoid bone.

HYOID FRACTURES

Although the most important lesions of the hyoid apparatus are the fractures, even with direct trauma, these are unusual. This is because the hyoid does not articulate with any other bone, is protected by soft tissue, and is freely moveable. Slack[5] gives the incidence as 0.002 per cent of all fractures. Hyoid fractures may be classified into two main groups: direct trauma due to an outside force, and muscular fractures.

Direct trauma includes those due to inward compression, such as manual strangulation; those secondary to anteroposterior compression, such as hanging or direct blows to the neck; and a miscellaneous category which includes bullet wounds.[15,27] In a study in the medical-legal literature[27] the hyoid was found fractured in 7 of 14 cases of manual strangulation, 9 of 33 cases of hanging, and 1 of 2 cases of ligature strangulation.

Mandibular fractures may be accompanied by fractures of the hyoid bone. This is more common than suspected and a hyoid fracture should be sought in such situations. Figure 12, *A* and *B* demonstrates an inward fracture of the midportion of the left greater cornu of the hyoid bone in a patient who also had a compound fracture of the left angle of the mandible. Instead of the normal gentle curvature of the greater cornu, evident on the right

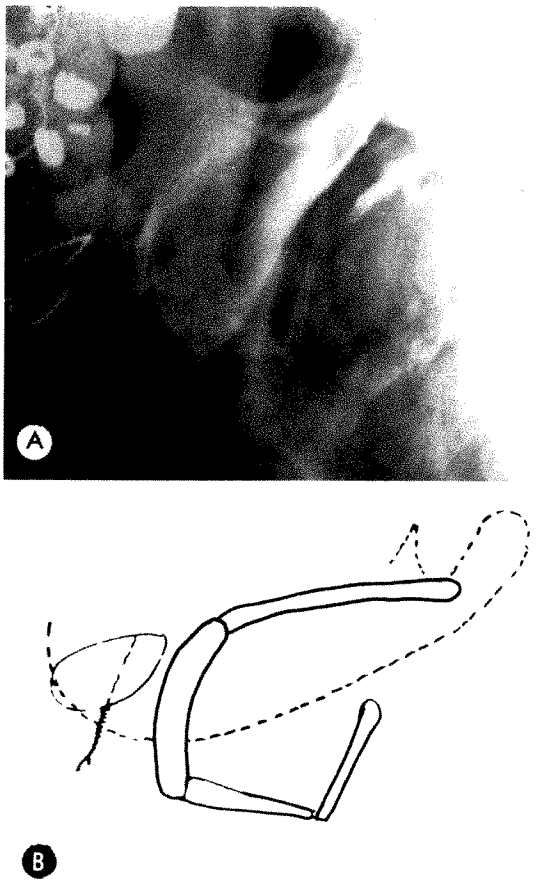


FIG. 12. (*A*) Inward fracture of midportion of left greater cornu of hyoid bone. Wire around mandibular fracture. (*B*) Line drawing of *A*.

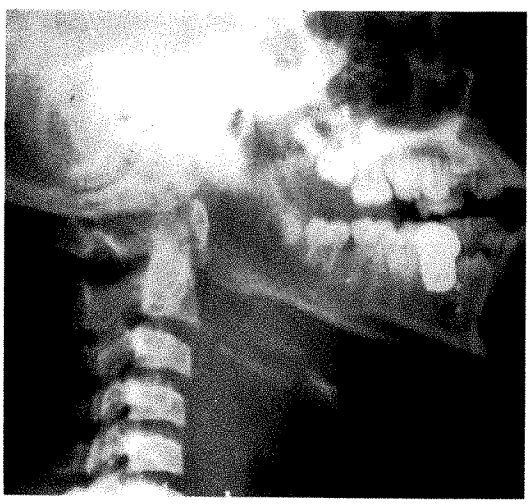


FIG. 13. Fracture of midportion of the right greater cornu of the hyoid bone. A bullet is lodged in the floor of the mouth. The mandibular fracture and transverse process fracture are not well seen in this projection.

side, there is discontinuity of the left cornu with an inward displacement of the posterior portion.

Roentgen examination of a 13 year old girl with a bullet wound to the neck showed fractures of the right transverse process of the fifth cervical vertebra, the right greater cornu of the hyoid bone, and the body of the mandible (Fig. 13).

There has been an increasing number of reports of hyoid fractures occurring in high velocity automobile and motorcycle accidents.[19] A 14 year old boy riding in the front seat of an automobile was thrown against and through the windshield. He sustained multiple lacerations to the scalp and facial area. The extent to which the head and neck went through the windshield is difficult to document since the child was unconscious. However, because lacerations were not noted below the mandibular ridge, it is probably safe to assume that this was the extent of the exit. The



FIG. 14. Superior displacement of the body of the hyoid bone in relation to the greater cornua as the result of a "muscular fracture." Compare with Figure 1*A*. Note also the alignment of the greater cornu in comparison to the mandibular rami.

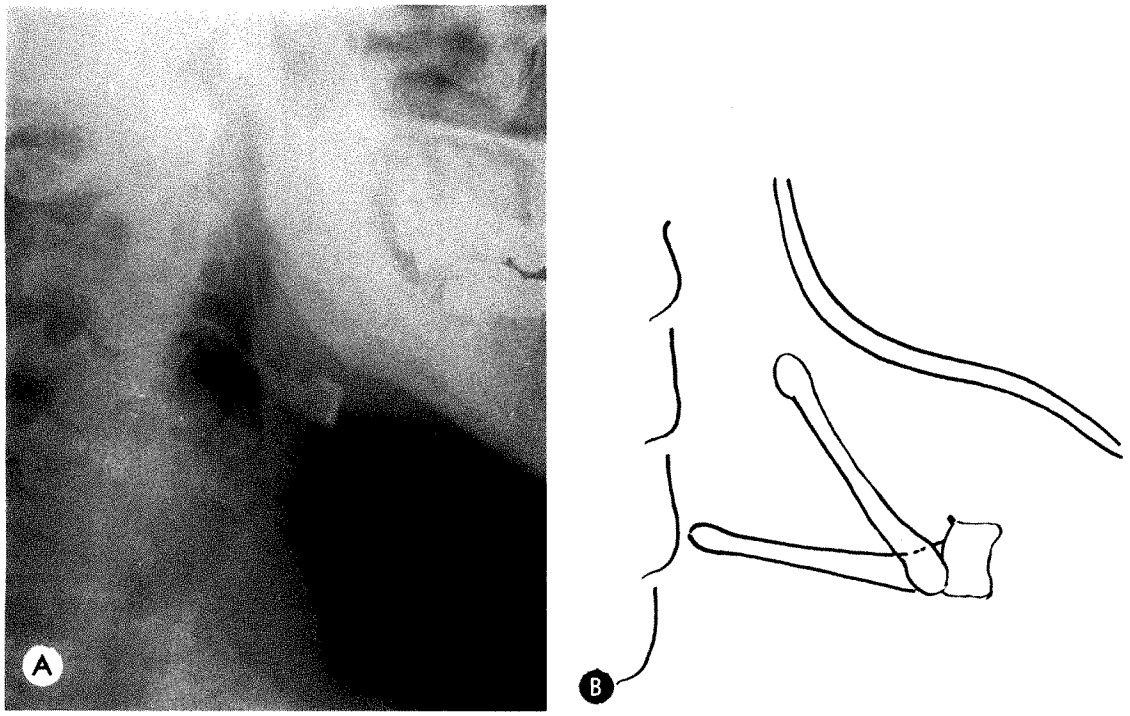


Fig. 15. (*A*) Fracture through the junction of the greater cornu and body with displacement of the cornu. Compare with Figures 1 and 14. (*B*) Line drawing of *A*.

neck showed no evidence of direct trauma in the form of lacerations, bruises or swelling. On roentgen examination of the neck, superior displacement of the body of the hyoid bone in relation to the greater cornua was noted (Fig. 14). Comparison with the normal alignment of the body and the greater cornua further clarifies the abnormality (Fig. 1*A*).

Although there is no direct clinical proof, it is likely that this represents a tear of the fibrous junction of the greater cornua and the body with displacement. The etiology of this is probably the sudden hyperextension and thrust that occurred at the time of the accident, with a "muscular fracture" resulting.[15,19]

Muscular fractures of the hyoid bone were recognized clinically prior to the discovery of x-ray.[15] The first such reported fracture was by Olliver de Angers before 1860. A muscular fracture occurs with sudden hyperextension of the neck, force being exerted by the contracting muscle groups upon the body and greater cornua of the hyoid.

Reimann[19] feels that older people have poor muscle coordination and are more susceptible to muscular fractures. These may occur from electrical shock, falls, and violent coughing and sneezing.

Figure 15, *A* and *B* demonstrates the presence of a fracture through the junction of the greater cornu and body. There is a superior displacement of the posterior portion of the cornu and inferior displacement of the anterior portion in relation to the body. The greater cornua of the hyoid normally parallel the rami of the mandible. When, as in this case, the rami of the mandible are almost superimposed, the greater cornua should be in the same plane.

A roentgenographic diagnosis of fracture of the hyoid bone may be difficult. There may be discontinuity of a cornu (Fig. 12, *A* and *B*), a fracture line (Fig. 12, *A* and *B*; and 13), or displacement of a cornu (Fig. 14; and 15, *A* and *B*). On oblique roentgenograms of the mandible or cervical spine the greater cornua of the hyoid do not lie in the same plane (Fig. 12, *A* and *B*). Comparison of the alignment of the cornua

with that of the mandibular rami, as demonstrated in the lateral roentgenogram, allows for better detection of fractures. Care must be taken to exclude lucencies caused by the superimposed pharynx. A triticeous cartilage present in the lateral hyothyroid ligament should not be mistaken for an avulsed fracture of the cornua (Fig. 1*B*). The lesser cornua may not be completely ossified and may appear displaced from the body (Fig. 1*A*; and 6). There are no cases in the literature of fractures of the lesser cornua. The greater cornua do not fuse with the body until the 35th or 45th years and occasionally not at all. Prior to this a fibrous junction persists.

Symptoms and signs that may arise from a fractured hyoid bone include tumefaction, bloody sputum, hoarseness, pain in the throat and neck aggravated by phonation or deglutition, and voice changes.[11]

The treatment of fractures depends upon the presence of laryngeal perforation. If the larynx has been punctured, as evidenced by indirect laryngoscopy, reduction of the fracture fragments should be performed. A tracheostomy may be necessary. Without perforation conservative therapy may be sufficient. This includes limitation of phonation and liquid diet. Prognosis of hyoid fractures is good. Nonunion of the fragments does not cause any decrease in function.[11,15,16]

SUMMARY

Anomalies and traumatic conditions of the hyoid bone are discussed. The anomalous junction between the greater cornua of the hyoid bone and the cornua of the thyroid cartilage is considered an atavistic occurrence of no clinical significance. Fractures of the hyoid bone may be due to direct trauma or secondary to muscular pull. The recognition of hyoid fractures as well as the pitfalls in diagnosis require an appreciation of normal roentgen anatomy. An attempt has been made to present the normal roentgen anatomy as well as the variations that may occur.

23101 Sherman Way
Canoga Park, California 91304

I would like to thank Doctors Harry Goldblatt and Erwin Haas for their assistance in translations, and Doctors Stephen Weiner and Frank Sherman for their editorial corrections and comments.

REFERENCES

1. ALBERS, G. D. Branchial anomalies. *J.A.M.A.*, 1963, *183*, 399–409.
2. AREY, L. B. Developmental Anatomy: A Textbook and Laboratory Manual of Embryology. Sixth edition. W. B. Saunders Co., Philadelphia, 1954.
3. BROWN, L. A. Hyoid bone syndrome. *South. M. J.*, 1954, *47*, 1088–1091.
4. CAFFEY, J. P. Pediatric X-Ray Diagnosis: A Textbook for Students and Practitioners of Pediatrics, Surgery and Radiology. Fourth edition. Year Book Medical Publishers, Chicago, 1961.
5. CHRISTOPHER, P. A Textbook of Surgery. Third edition. W. B. Saunders Company, Philadelphia.
6. DUMONT, L. Présentation de pièces: hyoides fractures. *Ann. méd. lég.* Sept.-Oct. Paris, 1962, *42*, 467.
7. EAGLE, W. W. Symptoms, diagnosis, and treatment of elongated styloid process. *Am. Surgeon*, 1962, *28*, 1–5.
8. FORMAN, F. S. Elongated styloid process. *Rocky Mountain M. J.*, 1964, *61*, 43–46.
9. GOSSEREZ, M., MALRAISON, P., and TREHEUX, M. Anomalie thyro-hyoïdienne. *J. de radiol. et d'élect.*, 1958, *39*, 194–198.
10. GROSSMAN, J. W. Triticeous cartilage: roentgen anatomic study. AM. J. ROENTGENOL. & RAD. THERAPY, 1945, *53*, 166–170.
11. GUERNSEY, L. H. Fractures of hyoid bone. *J. Oral Surg.*, 1954, *12*, 241–246.
12. HRISYIC-SOJIC, L., DUMONT, G., DEHOUVE, A., PROTEAU, J., and DEROBERT, L. À propos de fractures méconnues de l'os hyoïde. *Ann. méd. lég.*, 1963, *43*, 449–460.
13. KLINEFELTER, E. W. Anomalous hyoid: review of literature and report of case. *Radiology*, 1952, *58*, 224–227.
14. NELSON, L. A. Hyoid bursitis. *Texas J. Med.*, 1940, *36*, 435.
15. OLMSTEAD, E. G. Fractures of hyoid bone: presentation of two cases with review of literature. *Arch. Otolaryng.*, 1949, *49*, 226–274.
16. PAPAVASILIOU, C. G., and SPEAS, C. J. Fracture of hyoid bone. *Radiology*, 1959, *72*, 872–874.
17. PENDERGRASS, E., SCHAEFFER, J. P., and HODES,

P. The Head and Neck in Roentgen Diagnosis. Second edition. Charles C Thomas, Publisher, Springfield, Ill., 1956.

18. POPPEL, M. H., and CHRISTMAN, R. O. Fracture of hyoid bone: presentation of one case. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1956, *76*, 1144–1145.
19. REIMANN, W. Zungenbein und Schildkieferbrüche beim Verkungsunfallgeschehen. *Deutsche Ztschr. ges. gerichtl. Med.*, 1961, *52*, 70–75.
20. SAWWAF, B. Personal communication.
21. SERRATICE, M., FABRE, M., and VALERY, B. À propos de quatre cas d'appareil hyoïdien complet. *Rhumatologie*, 1962, *14*, 57–60.
22. SILVERMAN, F. N. Dysplasies epiphysaires: entité proteiforme. *Ann. radiol.*, 1961, *4*, 833–867.
23. SISSON, S. The Anatomy of Domestic Animals. W. B. Saunders Company, Philadelphia, 1935.
24. STAFNE, E. C., and HOLLINSHEAD, W. H. Roentgenographic observations on stylohyoid chain. *Oral Surg.*, 1962, *15*, 1195–2000.
25. TOMPSETT, A. C., JR., and DONALDSON, S. W. Anterior tubercle of first cervical vertebra and hyoid bone: their occurrence in newborn infants. AM. J. ROENTGENOL. & RAD. THERAPY, 1951, *65*, 582–584.
26. WARD, G. E., HENDRICK, J. W., and CHAMBERS, R. G. Thyroglossal tract abnormalities, cysts and fistulas: report of 105 cases from Johns Hopkins Hospital observed during the years 1926–1946. *Surg., Gynec. & Obst.*, 1949, *89*, 727–734.
27. WEINTRAUB, C. M. Fractures of hyoid bone. *Medicoleg. J.*, 1961, *29*, 209–216.

THE MANAGEMENT OF CERVICAL LYMPH NODE METASTASIS BY MEGAVOLTAGE RADIOTHERAPY*

By G. E. HANKS, M.D.,† M. A. BAGSHAW, M.D., *and* H. S. KAPLAN, M.D.
PALO ALTO, CALIFORNIA

THE purpose of this retrospective study is to determine the efficacy of megavoltage irradiation as the primary modality in sterilizing cervical lymph node metastases from squamous cell cancers of the head and neck. Million *et al.*[5] have reported 5 year survivals for carcinomas of the tongue, tonsil and nasopharynx associated with clinical lymphadenopathy, and Fletcher and Lindberg[2] have reported 18 month or more survivals for neoplasms of the tonsillar area, palate and retromolar trigone associated with clinical lymphadenopathy. In both of these studies, a failure in the neck was uncommon when the primary neoplasm was controlled, although the lymph node metastases were manged by a variety of means, *i.e.*, radiotherapy alone, radiotherapy plus surgery, and surgery alone. The present study differs in that all of the patients were treated initially by megavoltage radiotherapy to both the primary neoplasm and the involved lymph nodes. Surgery was reserved for treatment of persisting or recurrent neoplasm.

MATERIAL

The T-N-M staging systems outlined in Tables I and II were used for clinical classification of the extent of the primary tumors and of lymphadenopathy.

From January, 1956 to December, 1964, 94 patients with primary carcinomas of the head and neck and N-2 or N-3 adenopathy were evaluated for radiotherapy. Ten of these patients were not accepted for curative treatment because of concurrent medical illness, distant metastases, or second malignancies and therefore they are not included in the calculation of survival data. All patients have been followed in the conjoint Radiotherapy-Surgery Head and Neck Tumor Clinic, and/or in collaboration with their private physicians, and no patient has been lost to follow-up.

TABLE I

CERVICAL LYMPH NODE STAGING

N-0	No palpable lymph nodes
N-1	Single moveable lymph node less than 3 cm. in diameter
N-2	Multiple unilateral or single lymph node 3 cm. or larger in diameter
N-3	Fixed unilateral or bilateral lymph nodes

TREATMENT

A. GENERAL TECHNIQUES

External irradiation was given by the 4.8 mev. Stanford Medical Linear Accelerator, fabricated in the Stanford University Microwave Laboratory and installed in January, 1956.[4]

During radiation therapy the patients were seated in a special chair facing a vertical post to which a "bite-block" was affixed (Fig. 1). The bite-block was moulded from Kerr Dental Wax for each patient and served both to immobilize the head and also to guarantee reproducible positioning.[1,4] Thus potential difficulties of matching opposing lateral face fields with anterior and posterior opposed neck fields were minimized. Where the edges of adjacent fields abut in the area of metastases in the neck, the match lines were

* Presented at the Forty-ninth Annual Meeting of the American Radium Society, Toronto, Ontario, Canada, May 29–31, 1967.
From the Department of Radiology, Stanford University School of Medicine, Palo Alto, California.
This work was partly supported by Grants CA-05838 and CA-05008 from the National Cancer Institute, National Institutes of Health.
† Present Address: Department of Radiology, University of North Carolina Medical Center, Chapel Hill, North Carolina.

shifted periodically to ensure homogeneity of dosage. The incorporation of a diagnostic roentgen-ray tube within the collimator permitted easy verification of field shape and position by image intensification fluoroscopy. This was particularly advantageous in shaping fields to protect the spinal cord. Treatment field verification roentgenograms of diagnostic quality were obtained frequently for each patient.

Accessory lead blocks for precise shielding and beam shaping and/or wedge filters were attached to the front of the beam collimator (Fig. 2).

TABLE II

CLINICAL STAGING SYSTEM

A. CARCINOMA OF THE NASOPHARYNX	
T-1	Tumor limited to one site of the nasopharynx
T-2	Tumor extending into two sites of the nasopharynx
T-3	Tumor extending beyond the nasopharynx
B. CARCINOMA OF THE OROPHARYNX	
T-1	Tumor limited to one site of the oropharynx
T-2	Tumor extending into two sites of the oropharynx
T-3	Tumor extending beyond the oropharynx
C. CARCINOMA OF THE HYPOPHARYNX	
T-1	Tumor limited to one site of the hypopharynx
T-2	Tumor extending into two sites of the hypopharynx
T-3	Tumor extending beyond the hypopharynx
D. CARCINOMA OF THE LARYNX	
Stage I	Tumor limited to one anatomic site
Stage II	Tumor limited to one anatomic region
Stage III	Tumor extending beyond one anatomic region but confined to the larynx
Stage IV	Tumor extending beyond the larynx
E. CARCINOMA OF THE ORAL CAVITY	
T-1	Tumor less than 2 cm. in diameter
T-2	Tumor 2 to 4 cm. in diameter with minimal extension to adjacent structures
T-3	Tumor more than 4 cm. in diameter with limited or moderate extension to adjacent structures
T-4	Massive primary tumor

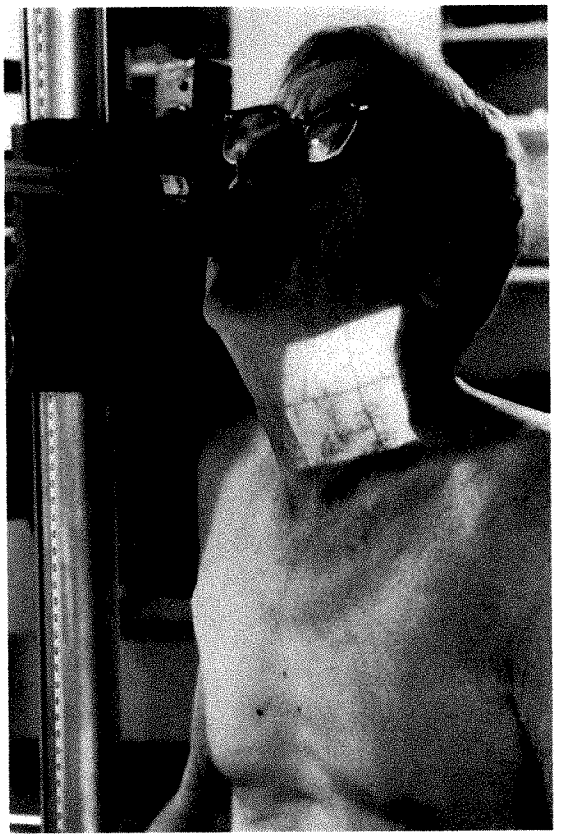


FIG. 1. Patient sitting in treatment position, immobilized by the dental wax bite block attached to calibrated pole. The image intensifier is visible in the background and the treatment field is delineated by the light beam.

B. TREATMENT TECHNIQUES; CARCINOMA OF THE NASOPHARYNX

The primary tumor is treated with opposing lateral fields shaped to include the nasopharynx, base of skull, sphenoid sinus, Eustachian tube, upper retropharyngeal lymph nodes, and posterior nasal cavity (Fig. 3, *A* and *B*). When the tumor is in the anterior nasopharynx or has invaded the posterior nasal cavity, one-half or more of the dose is delivered through a direct anterior portal. The primary site is treated to a mid-plane dose of 6,500 to 7,500 rads at a dose rate of 1,100 rads per week. Treatment in excess of 6,500 rads is given with fields of reduced size.

Bilateral neck irradiation is routinely administered through anterior and posterior opposed fields extending from below

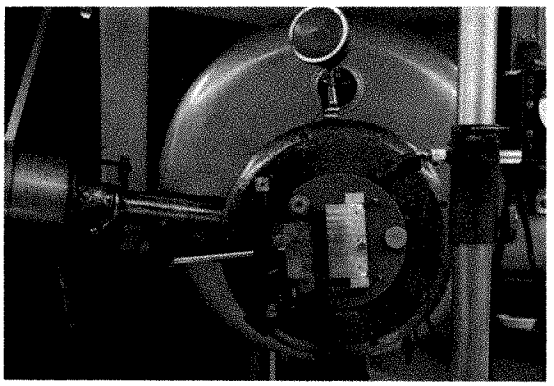


FIG. 2. A view of the front of the accelerator. The retractable diagnostic tube is seen on the left, a cervical spine block and wedge filter are attached to the front of the machine.

the clavicle to the mastoid process. A steel bar 2 cm. wide and 5 cm. thick (10 per cent transmission) is used to protect the midline pharyngeal structures and the spinal cord. The isodose distribution through a cross-section of the mid-neck indicates that dose is homogeneous to within ±7 per cent when the desired dose is calculated at the 75 per cent isodose line (Fig. 4). When the neck lymph nodes are clinically involved,

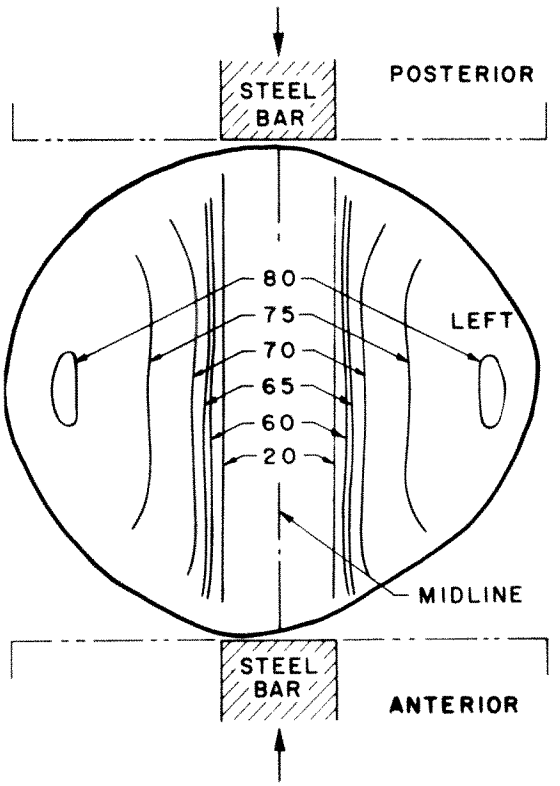


FIG. 4. Isodose distribution through the mid-neck produced by anterior and posterior opposed tangential neck fields with a mid-line steel bar.



FIG. 3. (*A* and *B*) Localization and portal verification roentgenograms demonstrating the volume irradiated in a carcinoma of the roof of the nasopharynx. Note the excellent technical quality of portal roentgenograms obtained with the diagnostic tube in the accelerator housing.

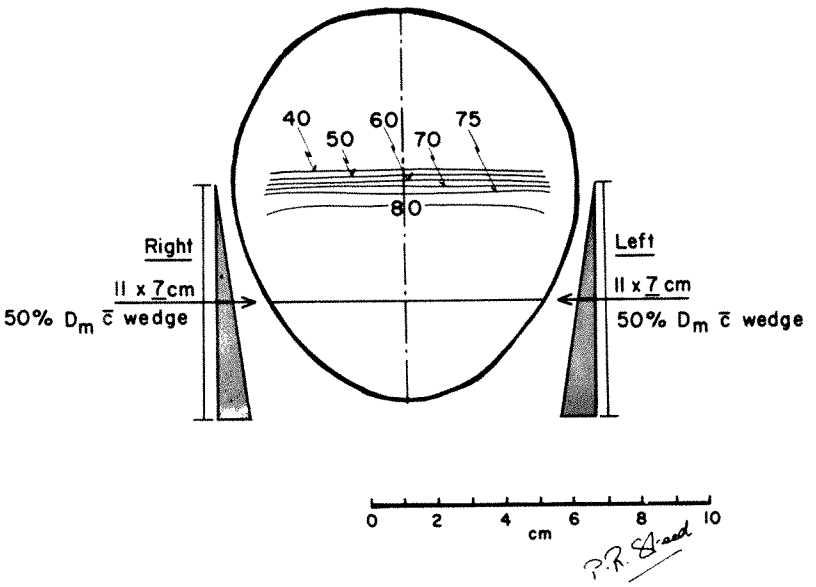


FIG. 5. Isodose distribution for opposing lateral fields directed at the hypopharynx. Homogeneous dose distribution is obtained by using bilateral wedge filters for 50 per cent of the treatment.

6,500 to 7,500 rads are delivered; when the neck is clinically negative, it receives 6,000 rads. All radiation is delivered at the rate of 1,100 rads per week, and a dosage above 6,500 rads is given with fields of reduced size.

C. TREATMENT TECHNIQUES FOR CANCER OF HEAD AND NECK; PRIMARY SITES OTHER THAN THE NASOPHARYNX

Because of the multiple primary sites, treatment plans are discussed in general terms. The primary lesion is usually treated with generous opposing lateral fields, or with intersecting wedged fields. These wedged fields may be at right angles when the lesion is well lateralized, or directly opposing as illustrated in Figure 5. The primary lesion and clinically involved lymph nodes are given between 6,500 and 7,500 rads. Clinically uninvolved lymph nodes receive a total dose of 6,000 rads. All treatment is given at 1,100 rads per week. The spinal cord is protected after 4,000 to 4,500 rads have been delivered. Supplementary interstitial therapy is used occasionally.

Lymph node areas not included in the primary fields are irradiated by anterior and posterior opposed fields to one or both sides of the neck as indicated by the primary lesion and its extension. When a unilateral neck field is irradiated, 35° wedge filters are used to improve the isodose distribution (Fig. 6). This distribution may be improved further by changing the position of the wedge on alternate days ("flip-flop" technique). In this technique, the wedge compensates for the slope of the neck on one day, while on alternate days it is positioned to compensate for the slope from the supraclavicular area to the neck (Fig. 7).

RESULTS

A. CARCINOMA OF THE NASOPHARYNX

Fifteen patients were accepted for curative therapy whose primary carcinomas were confirmed histologically as either squamous cell carcinomas or lymphoepitheliomas. In addition, 13 of the 15 patients had cervical lymph node metastases proven by biopsy prior to radiotherapy.

The staging of the primary neoplasm is indicated in Table IIA and of the lymph node metastases in Table I. The actuarial 5 year survival (uncorrected for natural attri-

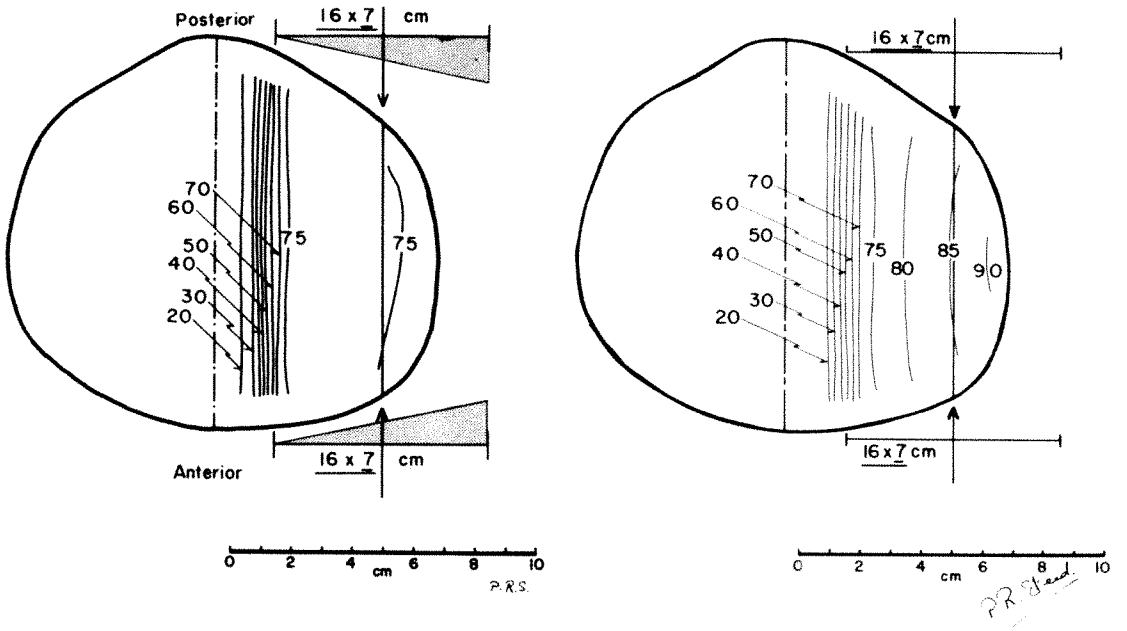


FIG. 6. Isodose distributions for unilateral cervical lymph node irradiation by anterior and posterior opposed fields. Dose homogeneity is greatly improved by the use of wedge filters.

tion) for this group was 66 per cent. Table III shows the importance of the extent of the primary lesion in prognosis. Two out of 3 T-3 patients died with neoplasm while 9 of 12 T-1 and T-2 patients survived. There was no instance of failure to control cervical

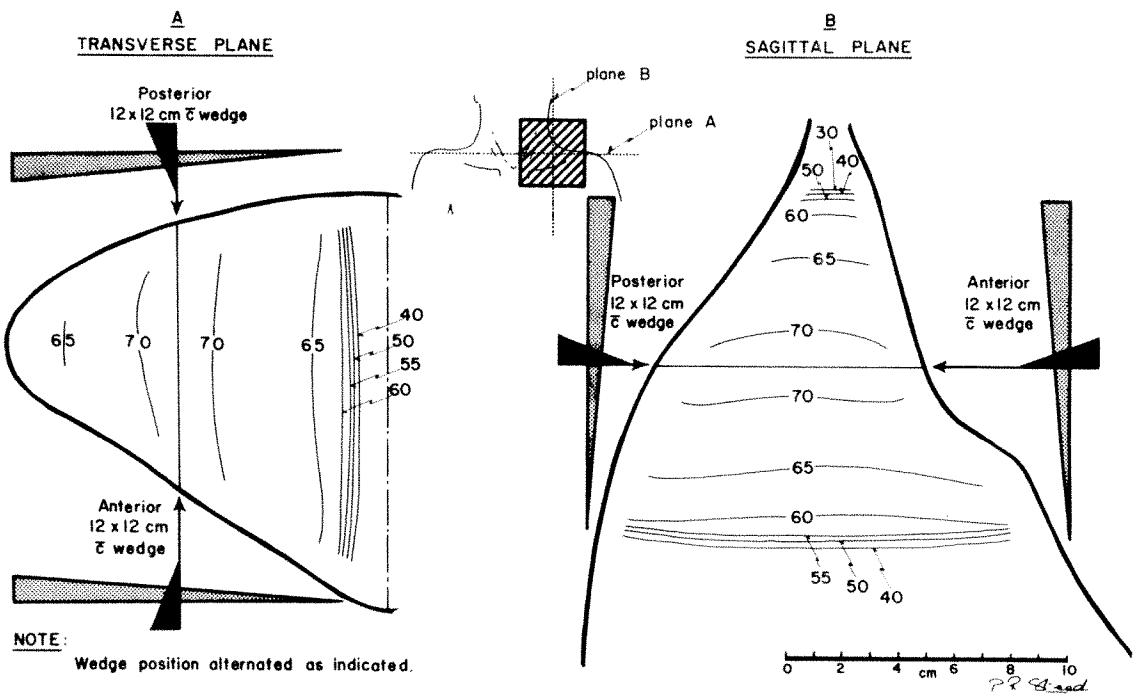


FIG. 7. "Flip-flop" technique isodose distribution: Alternating wedges produce a homogeneous dose distribution at the junction of the slopes of the neck and supraclavicular area.

TABLE III

CARCINOMA OF THE NASOPHARYNX
Patients alive 2 to 5 years after radiotherapy
(January 1956–December 1964)

	N-2	N-3	Total
T-1	1/2	3/4*	4/6
T-2	3/3	2/3	5/6
T-3	—	0/3†	0/3

Over-all survival 60 per cent.
* Patient died of distant metastasis with regional control.
† One patient died of cerebral thrombosis 34 months after radiation therapy with regional control.

lymph node metastases when the primary lesion was controlled.

B. CARCINOMA OF THE HEAD AND NECK EXCLUDING NASOPHARYNX

Sixty-nine other patients with N-2 or N-3 lymphadenopathy associated with previously untreated squamous cell carcinomas, primary in the head and neck region, were accepted for curative therapy. The clinically positive lymphadenopathy was confirmed by biopsy in 30 per cent of the cured patients and 23 per cent of those who died. The distribution of primary sites and therapeutic results are shown in Table IV. The uncorrected actuarial 5 year survival was 26 per cent (Fig. 8).

C. SITES OF FAILURE

Table V indicates the outcome for all patients excluding cancer of the nasopharynx. The most common cause of failure was inability to control both the primary lesion and the lymph nodes. However, the primary site alone appeared to be the source of

TABLE IV

A. CARCINOMA OF THE HYPOPHARYNX
Patients alive 2 to 5 years after radiotherapy
(January 1956–December 1964)

	N-2	N-3
T-1	—	0/1
T-2	0/1	1/3
T-3	1/4*	2/9

Over-all survival 22 per cent.
* Two patients died with intercurrent disease 23 months, and 25 months with no recurrence.

B. CARCINOMA OF THE TONGUE
Patients alive 2 to 5 years after radiotherapy
(January 1956–December 1964)

	N-2	N-3
T-1	—	1/1
T-2	2/2	0/4
T-3	—	2/4*
T-4	—	0/4†

Over-all survival 33 per cent.
* Two died of distant metastasis with regional control at 8 and 16 months after treatment.
† One died of distant metastasis with regional control at 3 months after treatment.

C. CARCINOMA OF THE TONSILLAR AREA
Patients alive 2 to 5 years after radiotherapy
(January 1956–December 1964)

	N-2	N-3
T-1	1/2*	0/1†
T-2	1/1	0/2
T-3	—	2/8‡

Over-all survival 29 per cent.
* One patient died of distant metastasis at 13 months with regional control.
† One patient died of distant metastasis at 30 months with regional control.
‡ One patient died of cerebral thrombosis at completion of therapy.

D. CARCINOMA OF THE SUPRAGLOTTIC LARYNX
Patients alive 2 to 5 years after radiotherapy
(January 1956–December 1964)

	N-2	N-3
T-1	—	—
T-2	0/1	1/2
T-3	1/2	2/4
T-4	0/1	0/4*

Over-all survival 29 per cent.
* One patient died with distant metastasis 19 months after treatment with regional control. One patient died due to a second primary neoplasm 41 months after treatment.

E. MISCELLANEOUS SITES
Patients alive 2 to 5 years after radiotherapy
(January 1956–December 1964)

Alveolus	T-3	N-3	0/2
	T-4	N-2	0/1
Palate	T-2	N-2	1/2
	T-2	N-3	1/1
Floor of Mouth	T-2	N-2	0/1
	T-3	N-3	0/1

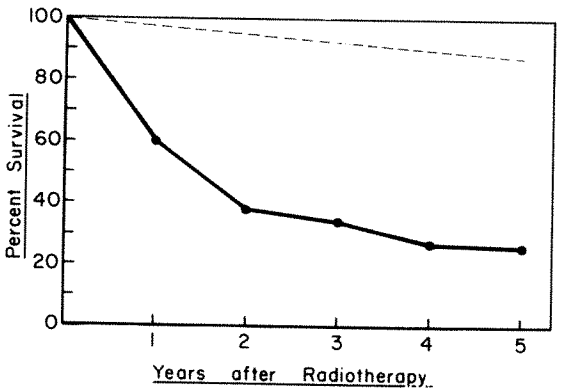


FIG. 8. Actuarial survival for 69 head and neck cancers with N-2 or N-3 cervical lymphadenopathy treated with irradiation (1956–1964). The actuarial survival calculation is not corrected for the 13 per cent expected natural attrition, this is indicated by the interrupted line.

failure in 8 patients whose lymph node metastases were controlled. One of these patients was salvaged by subsequent surgery, the remainder were not treatable or not cured by postirradiation treatment of the primary recurrence. Failure to control lymph node metastases by radiotherapy when the primary lesion was successfully eradicated occurred in only 2 of the 69 patients (3 per cent). One of these died because of persistent cervical and mediastinal metastases without evident neoplasm at the primary site. The other patient had a positive lymph node biopsy and a negative biopsy from the primary site in the pyriform sinus 5 months subsequent to radiotherapy. This patient expired of a hemorrhage from the pyriform sinus 1 month after radical neck dissection.

TABLE V

SITES OF FAILURE IN TREATING ADVANCED CARCINOMAS OF THE HEAD AND NECK

	No. of Patients	Per Cent
Primary lesion and lymph nodes not controlled	30	43
Primary lesion not controlled, lymph nodes apparently controlled	8	12
Distant metastasis with regional control	6	9
Intercurrent disease with regional control	4	6
Lymph nodes not controlled when primary lesion controlled	2	3
No failure	19	27
Totals	69	100

D. INACCURATE PRIMARY EVALUATION FOLLOWING RADIOTHERAPY

In 4 patients radical neck dissections disclosed neoplasm persistent in cervical lymph nodes, although the primary sites were negative by biopsy. However, between 2 and 4 months after surgery, positive biopsies were obtained from the primary site in each of these 4 patients. Fear of introducing local complications by performing extensive biopsies of heavily irradiated tissue contributed to the inaccurate evaluation of these cases. These data indicate that when the lymphadenopathy is not controlled by irradiation, the chances are great that the primary lesion is also not controlled. Therefore, subsequent surgery should encompass the primary site in addition to radical neck dissection.

E. COMPLICATIONS OF RADIOTHERAPY

The complications in these head and neck patients are summarized in Table VI. No significant complications occurred in 11 patients who survived for 2 years or more after treatment for carcinoma of the nasopharynx. In contrast, complications occurred in 6 (28 per cent) of 21 patients with

TABLE VI

COMPLICATIONS OF RADIOTHERAPY IN PATIENTS WITH ADVANCED HEAD AND NECK CANCER SURVIVING MORE THAN TWO YEARS

Carcinoma of the Nasopharynx	0/11
Other Head and Neck Cancers	
Laryngectomy for radiation chondritis	1/21
Severe fibrosis in the neck	1/21
Moderate fibrosis in the neck	2/21
Peripheral nerve injury	2/21
Total	6/21

tumors of various other primary head and neck sites surviving 2 years or more without local recurrence.

F. SECOND PRIMARY NEOPLASMS

One second primary neoplasm, a carcinoma of the prostate, was seen among 11 patients with cancer of the nasopharynx surviving 2 or more years. Six of 21 patients who survived for 2 or more years after irradiation for other head and neck cancers developed second primary carcinomas: 3 in the oral cavity, 2 of the esophagus, and 1 of the lung.

DISCUSSION

Only 4 of 15 patients (27 per cent) with advanced nasopharyngeal cancer developed recurrence in the primary site or the cervical lymph nodes after megavoltage radiotherapy by the techniques described. The chance of controlling the involved lymph nodes was identical with the ability to control the primary disease, as no patient had a lymph node recurrence in the absence of primary recurrence. Since all primary lesions in the nasopharynx must be treated radiotherapeutically, and since the lymph node metastases are equally radiosensitive, it is not logical to resect the lymph nodes. In addition, the cosmetic result following megavoltage irradiation of the neck is far superior to that following bilateral neck dissection.

The results in the other head and neck tumors demonstrate that irradiation was capable of controlling cervical lymph node metastases in 19 (27 per cent) of this group of 69 patients in whom radiation therapy was the exclusive primary treatment. Only 3 per cent of all patients were lost because of failure to control lymph node metastases when the primary was controlled, while 12 per cent were lost because the primary lesion alone was not controlled. Inability to control either the primary lesion or the lymph node metastases was the most common cause of failure (43 per cent). The actuarial 5 year survival of all patients is 26 per cent, a figure which agrees with the 28 per cent 5 year survival observed in 45 patients followed for 5 years. These data are comparable to the 21–27 per cent 5 year survivals reported by Million *et al.*,[5] for carcinoma of the tongue and tonsil with N-2 or N-3 cervical lymphadenopathy, and the 31–62 per cent 18 month or more results reported by Fletcher and Lindberg[2] for various neoplasms of the oral cavity presenting with N-2 and N-3 clinical lymphadenopathy.

A direct comparison between the results of radiotherapy and surgery in managing cervical lymph node metastases would be of vital interest. Henschke *et al.*[3] have reported a group of resectable head and neck cancers in whom a 3 year survival of about 66 per cent was obtained by surgery alone. Recurrence in the neck dissection site was noted in 16 of 39 (41 per cent) patients with unstaged but clinically palpable lymph nodes treated surgically. Similarly, neoplasm recurred in 21 per cent of the patients whose metastases were detected by microscopic examination only. Unfortunately, in this sub-group of Henschke *et al.*, it is impossible to identify the fraction of patients with recurrent disease in the neck only, nevertheless, their 41 per cent failure compares with our combined 46 per cent failure rate of 43 per cent primary and lymph node plus 3 per cent lymph node only. More meaningful are the data of Ogura and Powers,* who described the rate of recurrence in the neck 2 years following combined preoperative irradiation and surgery. In each of their patients metastases to the neck were proven histologically, and the primary tumor remained controlled by surgery. The cervical lymph node failure rates (by primary site) were: 1/17 (larynx), 2/14 (superior hypopharynx), 6/41 (hypopharynx). Despite the fact that cases with more advanced cervical lymphadenopathy are included in this report than in the surgical series cited, a comparison of the frequency of failure to control lymph node metastases when the primary lesion was controlled is

* Personal communication.

possible. Thus failure to control lymph node metastases in the presence of a cured primary neoplasm occurred in 13 per cent of Henschke and co-workers' patients,[3] 14 per cent of those reported by Fletcher and Lindberg,[2] 6–15 per cent of those presented by Ogura and Powers and in 3 per cent of the patients presented here. Since radiotherapy was thus as effective in controlling cervical lymph node metastases as it was in eliminating the primary neoplasm, and since the surgical reports cited show a similar or higher incidence of recurrence after resection of lymphadenopathy, it follows that when the primary neoplasm must be irradiated there is little justification for preferring resection to irradiation of the lymph nodes. Recognizing the success of radiotherapy in managing N-2 and N-3 cervical lymphadenopathy, even fewer failures might be anticipated in cases with N-0 and N-1 lymphadenopathy treated prophylactically by irradiation. This expectation has already been partially substantiated by Million *et al.*[5]

An analysis of our causes of failure suggests that an increased use of small volume local "boost" therapy to residual primary or lymph node tumor might increase cure rates. In addition, the high incidence of local failure in some cancers of the hypopharynx (T-1 and T-2 lesions with N-2 or N-3 lymphadenopathy, and all T-3 and T-4 lesions) has stimulated us to consider a clinical trial comparing the value of preoperative irradiation to that of surgery alone in randomly selected patients.

SUMMARY

1. Neoplasm recurrent within the irradiated volume was seen in only 4 of 15 patients with carcinoma of the nasopharynx metastatic to the cervical lymph nodes after treatment of both the primary neoplasm and the cervical metastases by megavoltage radiotherapy.

2. Nineteen of 69 patients with various other primary head and neck cancers associated with N-2 or N-3 clinical lymphadenopathy are free of tumor for 2 years or more (5 year survival rate 26 per cent) after treatment by radiotherapy alone.

3. Treatment failed in only 2/69 patients (3 per cent) because of inability to sterilize lymph node metastases when the primary neoplasm was controlled.

Gerald E. Hanks, M.D.
Department of Radiology
University of North Carolina Medical Center
Chapel Hill, North Carolina 27514

REFERENCES

1. BAGSHAW, M. A., SCHLIENGER, M., KAPLAN, H. S., and SAGERMAN, R. H. Linac radiotherapy V: cancer of laryngopharynx. *A.M.A. Arch. Otolaryng.*, 1965, *81*, 383–389.
2. FLETCHER, G. H., and LINDBERG, R. D. Squamous cell carcinomas of tonsillar area and palatine arch. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1966, *96*, 574–587.
3. HENSCHKE, U. K., FRAZELL, E. L., HILARIS, B. S., NICKSON, J. J., TOLLEFSEN, H. R., and STRONG, E. W. Value of preoperative x-ray therapy as an adjunct to radical neck dissection. *Radiology*, 1966, *86*, 450–453.
4. KAPLAN, H. S., and BAGSHAW, M. A. Stanford medical linear accelerator. III. Application to clinical problems of radiation therapy. *Stanford M. Bull.*, 1957, *15*, 141–151.
5. MILLION, R. R., FLETCHER, G. H., and JESSE, R. H., JR. Evaluation of elective irradiation of neck for squamous-cell carcinoma of nasopharynx, tonsillar fossa, and base of tongue. *Radiology*, 1963, *80*, 973–988.

VOL. 105, NO. 1

PRE AND POSTIRRADIATION AZYGOGRAPHY: ITS VALUE IN DETERMINING SURGICAL RESECTABILITY IN PULMONARY CARCINOMA*

By CARL T. RINKER, M.D., *and* ARCH W. TEMPLETON, M.D.†
COLUMBIA, MISSOURI

THE combination of azygography and superior vena cavography has been found to be of distinct value for the preoperative assessment of the resectability of pulmonary carcinoma.[2] The procedures are simple to perform requiring little specialized equipment, and the occurrence of complications is low. Azygography and superior vena cavography have been employed in 107 patients with suspected pulmonary carcinoma as part of their diagnostic work-up at the University of Missouri Medical Center. There have been no false negative studies and only one false positive study. The false positive study involved a patient with mediastinal fibrosis with resultant blockage of the azygos system.

Patients who manifested involvement of either the superior vena cava and/or azygos system were all found to have unresectable lesions as documented by thoracotomy. The value of the combined examinations is stressed, since it is impossible to predict which procedure will be of greatest value in a given case.

In light of the proven value of these examinations, azygography is now used to evaluate the effectiveness of radiation therapy. Patients were treated preoperatively to 2,000 rads tumor dose to the primary tumor and mediastinum in 4 treatments over a 1 week period. Anterior and posterior portals were used with a 1:1 loading utilizing the 2 mev. Van de Graaff unit. Reopening of the blocked azygos system documented by a repeat azygogram should indicate the reversal of an unresectable lesion to one that is resectable.

Eleven patients who were considered to have unresectable lesions following visualization of an abnormal azygogram had a repeat examination following the course of radiation therapy. These 11 cases will constitute the basis of this report.

TECHNIQUE

Azygography is performed in the anteroposterior and lateral positions using a biplane rapid film changing device. After infiltration with local anesthetic, a short beveled marrow needle is inserted into the marrow space of the 9th or 10th ribs in the midaxillary line on the side of the lesion. Following aspiration of bone marrow blood, a small amount of local anesthetic is instilled into the marrow space to reduce discomfort from the injection. Twenty cubic centimeters of 60 per cent meglumine iothalamate are injected manually over a 4 to 5 second period. Roentgenograms are taken near the end of the injection at the rate of 1 per second for 5 seconds with the patient breathing normally to obviate spurious blockage due to the increased venous pressure produced by the Valsalva maneuver.

Patterns of abnormality have been described previously[2] and are: (1) complete obstruction of the azygos or superior vena cava with no contrast material seen beyond the site of obstruction; (2) block of the azygos system with reconstitution beyond the site of obstruction; (3) displacement or deviation of either the azygos system or superior vena cava; (4) delayed emptying of the arch of the azygos vein indicating at least partial obstruction at the functional area of the azygos vein and superior vena cava; and (5) involvement of the superior

* Presented at the Fiftieth Annual Meeting of the American Radium Society, Miami Beach, Florida, April 7–11, 1968.
From the Department of Radiology, University of Missouri Medical Center, Columbia, Missouri.
Partially supported by USPHS Grant #CA08048.
† Present Address: Professor and Chairman, Department of Radiology, University of Kansas Medical Center, Kansas City, Kansas.

TABLE I

PATIENTS RE-EXAMINED BY AZYGOGRAPHY FOLLOWING RADIATION THERAPY

Findings at Azygography	Re-sectable	Unre-sectable
Reopening of the azygos system	5*	0
Continued partial or complete blockage of the azygos system	0	6

* Two of these patients had locally resectable lesions, but resection was not performed due to the presence of pleural implants.

vena cava and/or innominate veins distal to the entrance of the azygos vein.

Of the 11 patients given radiation therapy, 5 were considered to have surgically resectable lesions following the demonstration of a normal azygos vein. At thoracotomy the primary carcinoma was resectable in all cases although in 2 cases no resection was performed due to the finding of pleural involvement. The 6 patients with roentgenographic evidence of persistent partial or complete block of the azygos system had unresectable lesions at thoracotomy. Table 1 summarizes the results in this series.

DISCUSSION

The opening of a previously occluded azygos vein documented by repeat azygography 4 to 6 weeks following a course of preoperative irradiation provides a significant refinement for the management and prognosis of patients with pulmonary carcinoma (Fig. 1, *A* and *B*; and 2, *A* and *B*). These patients become candidates for thoracotomy and possible surgical extirpation. Patients who show persistent, partial or total occlusion may be given a more extensive course of radiation therapy. When radiation therapy is used as the primary modality of treatment, azygography may serve as a useful procedure for measuring progress and the efficacy of the extended therapy and may have some prognostic significance.

CONCLUSION

Eleven patients have had repeat azygography 5 to 6 weeks following a course of preoperative radiation therapy.

All patients showing reopening of the azygos system had a resectable primary

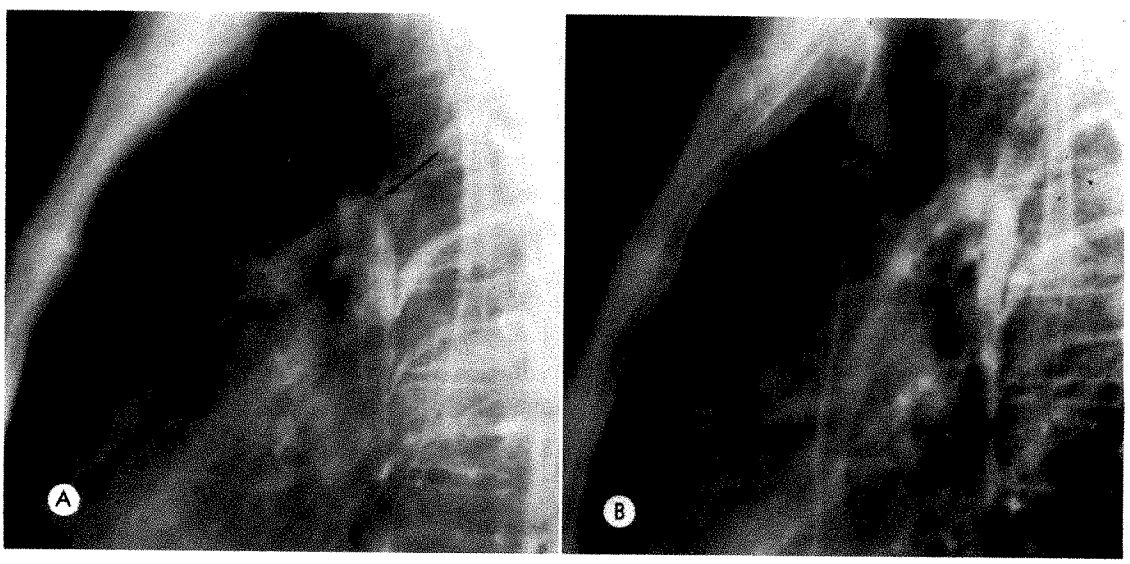


FIG. 1. (*A*) Lateral azygogram. The arrow points to the site of occlusion. (*B*) Lateral azygogram 6 weeks following radiation therapy. The azygos system has reopened. The lesion was resected and the patient is living without evidence of disease 16 months postresection.

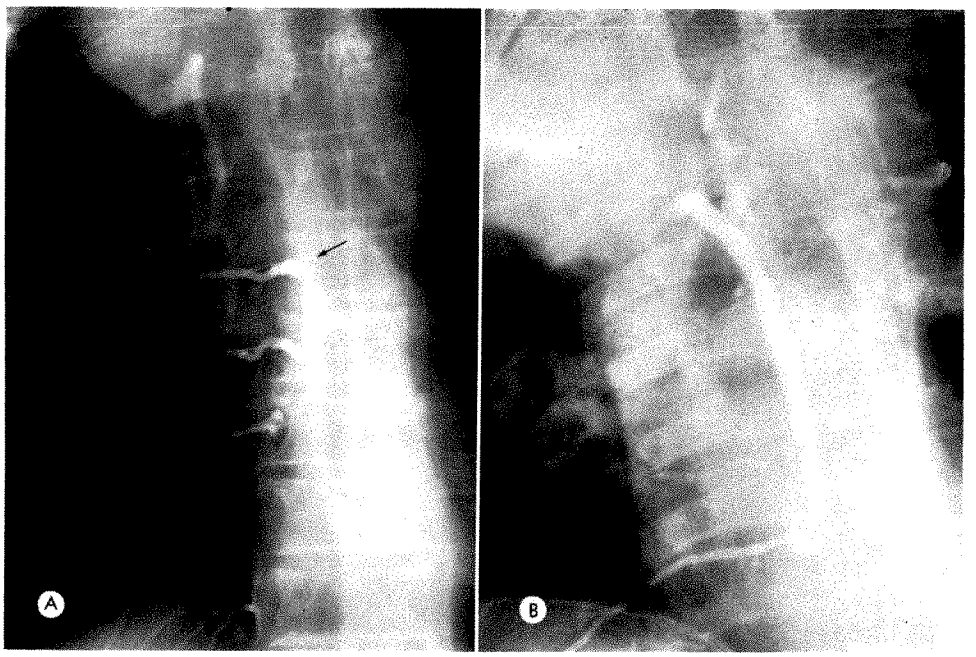


FIG. 2. (*A*) Anteroposterior azygogram. The arrow points to the site of occlusion in a 59 year old male with carcinoma of the right upper lobe. (*B*) Anteroposterior azygogram. The azygos vein is open following radiation therapy. The patient is without evidence of disease 31 months postresection.

lesion and all patients with continued occlusion of the azygos system had unresectable lesions.

The value and prognostic significance of repeat azygography following radiation therapy are discussed.

Carl T. Rinker, M.D.
Department of Radiology
University of Missouri Medical Center
Columbia, Missouri 65201

REFERENCES

1. JANOWER, M. L., DREYFUSS, J. R., and SKINNER, D. B. Azygography and lung cancer. *New England J. Med.*, 1966, *275*, 803–808.
2. RINKER, C. T., TEMPLETON, A. W., MACKENZIE, J., RIDINGS, G. R., ALMOND, C. H., and KIPHART, R. Combined superior vena cavography and azygography in patients with suspected lung carcinoma. *Radiology*, 1967, *88*, 441–445.
3. SKINNER, D. B., DREYFUSS, J. R., and NARDI, G. L. Azygography in evaluation of operability of pulmonary carcinoma. *New England J. Med.*, 1962, *267*, 232–237.
4. WOLFEL, D. A., LINBERG, E. J., and LIGHT, J. P. Abnormal azygogram: an index of inoperability. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1966, *97*, 933–938.

DEFINITIVE RADIOTHERAPY OF PRIMARY MEDIASTINAL SEMINOMA*

By MALCOLM A. BAGSHAW, M.D.,† WILLIAM T. McLAUGHLIN, M.D.,‡ *and* JOHN D. EARLE, M.D.§
PALO ALTO, CALIFORNIA

ALTHOUGH the pathogenesis of the rare primary mediastinal seminoma is obscure, its response to radiation therapy is similar to that of histologically identical neoplasms of testicular origin. Four of 6 patients with this lesion appear to have been successfully treated with megavoltage irradiation by means of the Stanford Medical Linear Accelerator.[5,8] Since Friedman[4] in 1951 called attention to the occurrence of extragenital seminomas originating in the anterior mediastinum, a number of other case reports have appeared in the literature. Kountz *et al.*[11] tabulated 25 recorded cases and added 4 from the Stanford series. A follow-up of the 3 patients reported by Kountz and his associates who were treated by radiation therapy, as well as an additional 3 patients treated at Stanford, will be presented. Molina and his co-workers[14] in 1965 reviewed the case reports and enlarged the list to 35. For the sake of completeness, we have summarized the reported cases in sufficient detail to abstract the method of treatment, radiation dose, and follow-up and have added 9 case reports, either not mentioned by Kountz *et al.*[11] or Molina *et al.*[14] or which have been published since their reports (Tables I, II and III). The 6 patients treated at Stanford were managed in a relatively uniform manner, and since this represents the largest single group to be treated by irradiation at one institution, it seems appropriate to try to define the radiotherapeutic approach.

While it is beyond the purview of this study to elaborate on the oncogenesis of this neoplasm, several different points of view have been presented. Schlumberger,[22,23] for example, suggested that extragonadal germinal tumors develop because of a dislocation of the germ layers during embryogenesis. Friedman[4] attributed the teratoid tumors of the thymus to displaced primordial germ cells and suggested that some of these may differentiate as germinomas (seminomas). Others have advanced the theory that primary testicular tumors may regress spontaneously while their metastases continue to grow. Azzopardi *et al.*[2] and Rather *et al.*[20] described well-defined fibrous scars in the testis after detailed histologic examination, which they believed represented the primary site in patients with disseminated gonadal tumors. One of the most important reasons that so few cases of this entity have been reported is the difficulty in separating this neoplasm histologically from other epithelial-like tumors of the thymus. Lattes,[13] for instance, submitted one of his cases to a panel of pathologists at the Penrose Cancer Seminar in 1960. Ninety-three pathologists diagnosed thymoma, 23 seminomatous thymoma, and 5 teratoma. One must agree with Nazari and Gagnon[15] who found that "this makes it difficult to have a universal classification for tumors of the thymus gland."

RESULTS

STANFORD EXPERIENCE

The clinical findings in mediastinal seminoma are those of a rapidly growing anteriormediastinal neoplasm. Initial manifestation of the tumor may be indicated by chest

* Presented at the Fiftieth Annual Meeting of the American Radium Society, Miami Beach, Florida, April 7–11, 1968.
From the Department of Radiology, Stanford University School of Medicine, Palo Alto, California.
Supported by grant CA 05838, National Cancer Institute, National Institutes of Health, USPHS.
† Associate Professor of Radiology and Director, Division of Radiation Therapy.
‡ Clinical Instructor in Radiology.
§ Fellow in Radiation Therapy.

TABLE I

TREATED WITH IRRADIATION ONLY

Author	Year of Report	Age, Sex	Pathology	Follow-up	Description of Treatment
Woolner *et al.*[27]	1955	24 M	Seminoma with lymphoid stroma	Dead 6 years	13 daily treatments after biopsy (inoperable): 3,600 r to mediastinum (1,800 r through each of 2 portals). Additional irradiation to metastases in spine, hips, legs, and groin
Effler and McCormack[3]	1956	30 M	Seminoma	Alive 9 years	250 kv., 3,200 r to skin of 2 portals crossfiring anterior mediastinum. Recurrence in cauda equina at 3 years: 250 kv., 2,500 r to skin of lower lumbar area and 1,400 r to an area in the left buttock region in a 2 month period
Effler and McCormack[3]	1956	32 M	Seminoma	Alive 6 years	Co^{60}, 3 portals, 3,500 r to skin of each portal with a tumor dose of 4,500 r. Re-treatment 1 year later: Co^{60}, 4,000 r to tumor through 3 portals
Robinson[21]	1960	35 M	Seminoma at first thought to be metastatic undifferentiated carcinoma	Alive 2 years	250 kv., half value layer 2.5 mm. Cu, 50 cm. target skin distance, 15×20 cm. anterior and posterior opposing mediastinal portals, 2,704 rads in 30 days tumor dose
Steinmetz and Hays[24]	1961	35 M	Seminoma	Dead 1½ years	Co^{60}, 3,000 r to superior mediastinum in 2 weeks; Co^{60}, 3,000 r to right tonsilar area in 2 weeks. Mediastinal recurrence: 3,180 r in 2 weeks to right hilum and mediastinum
*Kuznetsov *et al.*[12]	1961	30	Seminoma	Alive 10 months	Through grid over both regions of anterior mediastinum, 7,750 r; over supraclavicular region, 5,400 r
*Nazari and Gagnon[15]	1966		Seminoma	Alive 7 years 9 months	7,800 r tumor dose Co^{60}
*Kleitsch *et al.*[10]	1967	54	Seminoma	Dead 18 months. Intercurrent disease. No tumor, testes negative	250 kv., tumor dose 3,200 rads
*Bagshaw *et al.*	1968	33 M (H.M.W.)	Seminoma	Alive 7 years. No evident disease for past 3 years and 9 months	5 mev. Stanford linear accelerator, 8×10 cm. anterior and posterior opposing portals, extending from 1 cm. above sternal notch to diaphragm, 4,000 rads tumor dose in 36 days. Additional irradiation to metastases of left knee, left mandible, iliac and para-aortic lymph nodes
*Bagshaw *et al.*	1968	27 M (C.C.)	Seminoma	Alive 6 years 4 months	5 mev. Stanford linear accelerator, anterior and posterior irregularly shaped opposing portals including both supraclavicular areas and extending to the diaphragm, 4,000 rads tumor dose in 32 days
*Bagshaw *et al.*	1968	52 M (C.F.)	Seminoma in supraclavicular lymph nodes	Alive 1 year 3 months	5 mev. Stanford linear accelerator, mediastinal mass and supraclavicular lymph nodes treated *en bloc*, 3,500 rads in 40 days
*Bagshaw *et al.*	1968	21 M (A.O.)	Seminoma	Dead 7 months of disseminated metastases	5 mev. Stanford linear accelerator, 1,000 rads total chest field reduced to include mediastinum, axillae and supraclavicular lymph nodes; total to mediastinum, 3,500 rads in 30 days
*Bagshaw *et al.*	1968	56 M (S.L.)	Seminoma (cervical lymph node biopsy)	Dead 5 months of cerebrovascular disease and myocardial infarction. Probable disseminated neoplasm. No postmortem examination	5 mev. Stanford linear accelerator, 1,275 rads whole chest field reduced to include mediastinum and supraclavicular lymph nodes; total 3,510 rads in 29 days

* Cases not previously summarized by either Kountz *et al.*[11] or Molina *et al.*[14]

pain, dyspnea, or orthopnea, superior vena caval obstruction, cervical adenopathy, or weight loss. Two of our patients complained of vague chest discomfort, while in another, severe, sharp mediastinal pain was noted. In one of these patients, the mass enlarged rapidly, becoming both visible and palpable in the right parasternal region within 2

TABLE II

RESECTION FOLLOWED BY IRRADIATION

Author	Year of Report	Age, Sex	Pathology	Follow-up	Description of Treatment
Woolner *et al.*[27]	1955	31 M	Seminoma	Alive 7 years	Almost complete excision, followed by 6,000 r to mediastinum (1,500 r through each of 4 portals). Additional irradiation to metastases in skull, axilla, femur and spine
*O'Gara *et al.*[17]	1958	?	Seminoma	Alive 6 years	5,500 r to anterior mediastinum
Inada and Nakano[6]	1959	23 M	Seminoma	Alive 8 years	Complete resection plus postoperative irradiation with 250 r×4 days and repeated 1 month later
Audier *et al.*[1]	1960	30 M	Seminoma	Alive 3 years	Complete resection plus 4,800 r tumor dose in 12 weeks
Inada *et al.*[7]	1963	23 M	Seminoma, embryonal carcinomatous tissue in one area	Dead 130 days	Mass removed with portion of right upper and middle lobes. Co^{60}, 800 r preoperative and 2,200 r postoperative
*Oberman and Libcke[16]	1964	42 M	Seminoma	Alive 5 years	4,000 r (not detailed)
*Pachter and Lattes[18]	1964	46 M	Seminoma	Dead 6 months, large mediastinal recurrence	6,000 r in 5 months
Molina *et al.*[11]	1965	31 M	Seminoma	Alive 18 months	Initial resection not followed by irradiation. Superior mediastinal recurrence treated 6 months later: 5,700 r in 23 treatments. One year later required further irradiation to a different region in mediastinum
*Bagshaw *et al.*	1968	35 M (H.W.)	Seminoma ? teratocarcinoma	Alive 6 years 3 months	5 mev. Stanford linear accelerator, 6,000 rads in 53 days tumor dose to mediastinum and supraclavicular region

* Cases not previously summarized by either Kountz *et al.*[11] or Molina *et al.*[14]

weeks of its initial demonstration on chest roentgenograms. In two other patients the first symptoms were those of early superior vena caval syndrome with swelling of the face and minimal congestion of the vessels of the neck. In one of these patients dyspnea secondary to pleural effusion was also present. In one patient cervical lymphadenopathy was the initial manifestation, while in another there were no clinical findings, and the mediastinal mass was discovered on a routine chest roentgenogram. Although one patient complained of night sweats and fever, systemic signs and symptoms, other than weight loss, were not common.

Lymphangiography and inferior venacavography were performed in 5 of our 6

TABLE III

RESECTION ONLY

Author	Year of Report	Age, Sex	Pathology	Surgery	Follow-up
Pugsley and Carleton[19]	1953	16 M	Malignant teratocarcinoma with nodule of seminoma	Partial resection	Dead within 2 months
Woolner *et al.*[27]	1955	23 M	Teratocarcinoma with foci of seminoma	Surgical resection	Dead within 3 months; spinal cord compression
Taniguchi *et al.*[26]	1957	19 M	Seminoma	Resection	Operative death
Taniguchi *et al.*[26]	1957	18 M	Seminoma	Resection	Operative death
Kountz *et al.*[11]	1963	37 M	Seminoma-like tumor	Complete resection	Alive at 6 years
*O'Gara *et al.*[17]	1958	27 M	Seminoma	Complete resection	Alive at 17 years
*Lattes[13]	1962		Seminoma	Complete resection	Alive at $7\frac{1}{2}$ years
*Lattes[13]	1962		Seminoma or "seminoma like"	Complete resection	Alive at $4\frac{1}{2}$ years
Inada *et al.*[7]	1963	23 M	Seminoma	Complete resection	Alive at 8 years

* Cases not previously summarized by either Kountz *et al.*[11] or Molina *et al.*[14]

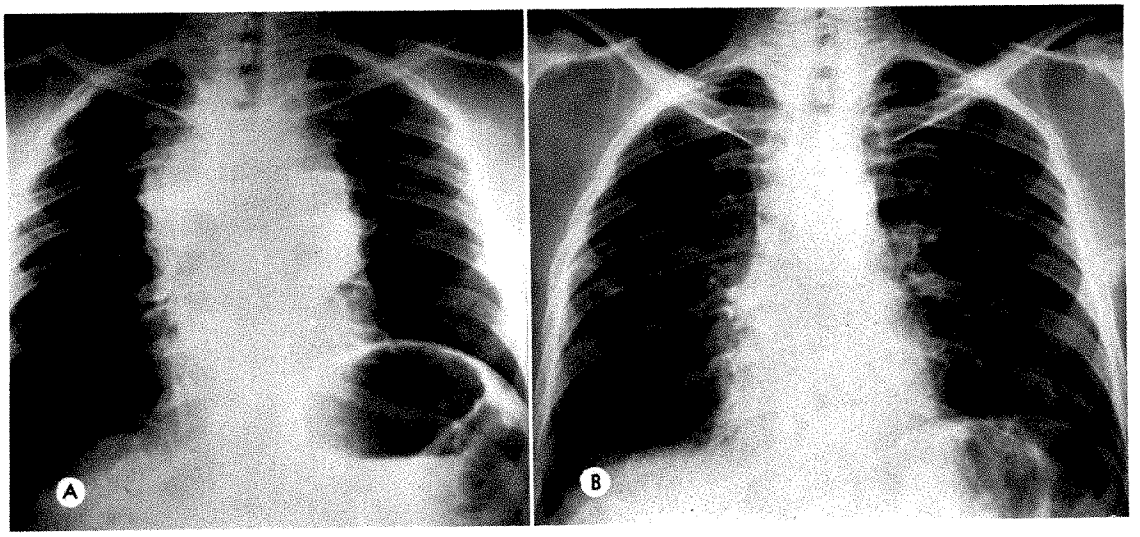


FIG. 1. (*A*) Posteroanterior chest roentgenogram obtained before open surgical biopsy. The large mediastinal mass bulges to each side. At fluoroscopy, the elevated left hemidiaphragm moved paradoxically with respiration. (*B*) Posteroanterior chest roentgenogram obtained 4 months after the beginning of irradiation. The large mediastinal mass has disappeared. There is residual slight elevation of the left hemidiaphragm and some streaking in the paramediastinal regions. The right pleural thickening present since open surgical biopsy has gradually improved. Although several metastatic sites have been treated (see Case Report), the patient is now well without evidence of disease at 7 years.

patients. The lymphangiogram and inferior venacavogram were both clearly positive in one patient demonstrating para-aortic lymphadenopathy in the region of the renal hilum. In another patient the lymphangiogram was negative, but 4 months later retained contrast medium in the para-aortic lymph nodes became displaced, suggesting para-aortic metastases. This change was proved to be due to neoplasm at postmortem examination. In a third patient para-aortic metastases were proven 3 years and 4 months after the initial mediastinal treatment, at which time the lymphangiogram was interpreted as normal. In the remaining 2 patients, the initial lymphangiograms were interpreted as equivocal, but para-aortic metastases were not verified at laparotomy. Thus, para-aortic lymph node metastases were present in 3 of these 6 patients, and in 1 the initial lymphangiogram demonstrated the involvement.

Testicular atrophy has been cited as a frequent finding in patients with primary mediastinal seminoma. In one of our patients atrophy was clearly evident, proven by testicular biopsy, and the patient had no desire for sexual activity. In two others the testes were normal on physical examination. In the remaining three, a minimal testicular atrophy was described; however, each of the patients had fathered one or more children.

Many of the features of mediastinal seminoma can be found in one of our patients, and it is worthwhile to recount his case in more detail.

REPORT OF A CASE

In February, 1961, the patient, a 33 year old unmarried male, complained of exertional dyspnea for $2\frac{1}{2}$ months and swelling of the face of 3 weeks' duration. For 2 weeks prior to admission he noted a "pressing pain" in the mid-chest which was aggravated by lying supine. A chest roentgenogram demonstrated a massive mediastinal mass (Fig. 1*A*). A mediastinal biopsy disclosed a classic seminoma (Fig. 2, *A* and *B*). He was treated with 4,000 rads in 36 days* through 18×10 cm. anterior and

* Unless otherwise stated, all patients were treated with either the Stanford Medical Linear Accelerator, which produces a 5 mev. roentgen-ray beam with an output of 80 rads per minute at 1 meter target skin distance, or with the Varian Clinac at 6 mev. with an output of 200 rads per minute at 1 meter target skin distance.

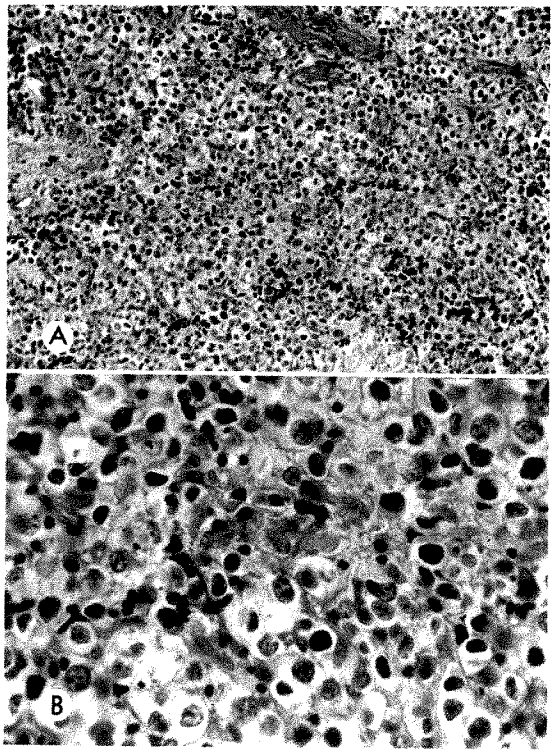


FIG. 2. (*A*) Low and (*B*) high power photomicrographs of biopsy specimen removed from patient illustrated in Figure 1, showing a typical seminomatous pattern. (Hematoxylin and eosin stain.)

posterior opposed shaped thoracic portals. He responded well to therapy with prompt relief of symptoms. By several weeks post treatment, the patient was asymptomatic (Fig. 2*B*). A lymphangiogram after the completion of therapy disclosed no abnormality.

The patient was well until April, 1962, at which time he developed pain in the left knee. Roentgenograms disclosed a lytic lesion of the proximal left tibia, and seminoma was proved by needle biopsy. A total of 3,675 rads in 26 days was given with relief of pain. In November, 1962, a lytic lesion of the left mandible was biopsied and proved to be metastatic seminoma. A total of 2,262 rads was given in 13 days. Both the tibia and mandible were treated by 280 kv., 20 ma. roentgen therapy. The dose was not carried higher because it was anticipated that the neoplasm was disseminating rapidly and palliative treatment was indicated. However, the lesion responded well, with the prompt relief of pain and lack of evidence of further bone destruction.

In April, 1963, an intra-abdominal mass was palpable in the pelvis. The patient had an episode of hematuria, and this was assumed to be another metastasis involving the urinary bladder. A total of 2,000 rads in 13 days was given to the mid-pelvic region.

In July, 1964, another abdominal mass was palpated. Exploration and biopsy disclosed seminoma confined to the para-aortic and iliac lymph nodes. The para-aortic lymph nodes were treated at first through a 22×23 cm. field, which was later reduced to 22×11 cm. The pelvis was treated through adjacent 22×22 cm. fields in order to include the iliac lymph nodes bilaterally. Thus, 2,950 rads in 44 days were given to treat retroperitoneal lymphadenopathy. At that time, although there was no palpable testicular tumor, the testes were explored, and a liberal biopsy from each was obtained. The biopsies failed to demonstrate seminoma.

The patient has had no further evidence of disease since July, 1964, and is now living and well 7 years after his initial treatment and 3 years and 9 months after treatment of his most recent metastases.

Comment. The histopathology of this tumor is characterized by solid sheets of large cells, subdivided into smaller nests by interlacing strands of fibrous tissue. The cells are uniform in appearance with pale or clear cytoplasm and oval or round nuclei generally centrally located within the cell. The nuclei contain densely clumped chromatin, usually well-defined nucleoli which tend to be slightly eosinophilic. Mitoses are frequent (Fig. 2, *A* and *B*).

A summary of the radiation dose and cur-

TABLE IV

PRIMARY MEDIASTINAL SEMINOMA: RESULTS OF RADIATION THERAPY IN 6 CASES

Case No.	Radiation Dose (5 mev.)	Status
1 (HMW)	4,000 rads, 36 days	NED,* 7 years
2 (CC)	4,000 rads, 32 days	NED,* 6 years 4 months
3 (HW)	6,000 rads, 53 days	NED,* 6 years 3 months
4 (CF)	3,500 rads, 40 days	NED,* 1 year 3 months
5 (AO)	3,500 rads, 30 days	Dead, 7 months
6 (JL)	3,510 rads, 29 days	Dead, 5 months

* NED = no evidence of disease.

rent status of each of the Stanford cases is presented in Table IV. The patient who was given 6,000 rads was treated to the higher dose because one of four pathologists interpreted the neoplasm as embryonal carcinoma; the others diagnosed seminoma. Although treatment failed in the 2 patients who were given only 3,500 rads, it is difficult to ascribe the failure to the dose because they developed rapidly progressive metastatic disease.

DISCUSSION

Extragonadal "germinal" tumors are being recognized with increasing frequency. Those which occur in the mediastinum often appear to grow rapidly, produce symptoms early, and are subject to relatively early diagnosis by simple chest roentgenography. Although the histologic type may vary, those with a seminomatous pattern should be recognized as a clinical entity and treated aggressively by both surgery and radiation therapy, since the prognosis for this subgroup is not as pessimistic as suggested by Pachter and Lattes.[18] These authors reported 10 benign teratomas, 8 malignant teratomas, 1 seminoma, and 5 choriocarcinomas which were primary in the mediastinum. Surgical resection was impossible in all of the malignant tumors, which were uniformly fatal. The one seminoma failed to be controlled by irradiation. However, the 6,000 r was delivered over a period of 5 months. The precise details of therapy were not reported. A comprehensive review of the literature (Tables I, II, III, and V) discloses that mediastinal seminoma, unlike malignant teratomas and choriocarcinomas, appears to be a curable lesion. Tables I, II and III present the recorded cases in which some details of therapy were presented and in which there was an indication of the therapeutic results. In Table V all the results are summarized. Sixteen of the total of 22 patients treated with total resection followed by radiation therapy, subtotal resection followed by radiation therapy, or radiation therapy alone were reported living from 1 to 9 years after treatment. Five of 9 patients treated by resection only are living from $4\frac{1}{2}$ years to 17 years following resection.

Study of Table VI indicates that the radiation doses employed in most of the successfully treated patients are between 3,000 and 6,000 rads, while the dose used in the unsuccessfully treated patients was usually less than 4,000 rads. Since it has been shown in the treatment of mediastinal lymphoma[9] that 4,000–4,500 rads to the mediastinum and supraclavicular region is well-tolerated, and since doses in excess of this may be associated with an increasing incidence of pericardial and myocardial damage,[25] it seems reasonable to select 4,000–4,500 rads delivered at the rate of 1,000 rads per week for the treatment of this en-

TABLE V

TREATMENT OF PRIMARY MEDIASTINAL SEMINOMA SUMMARY OF LITERATURE

Treatment	Living at Last Report	Dead
Resection plus irradiation	7	2
Biopsy only plus irradiation	9	4
Subtotal	16*	6
Resection only	5	4
Total	21	10
* Includes Stanford cases.	4	2

TABLE VI*

ESTIMATE OF DOSES EMPLOYED

Estimated Tumor Dose (×1,000 rads)	Number of Patients "Cured"	Not Cured
<2	1	—
2–3	1	1
3–4	5	3
4–5	4	—
5–6	4	1
>6	1	—

* These data are abstracted from Tables I, II and III. They are presented as the authors' best estimate of the doses employed, since in some instances precise data were not available. In other cases the irradiation followed gross total resection, and the contribution of radiation therapy to the status of the patient cannot be assessed.

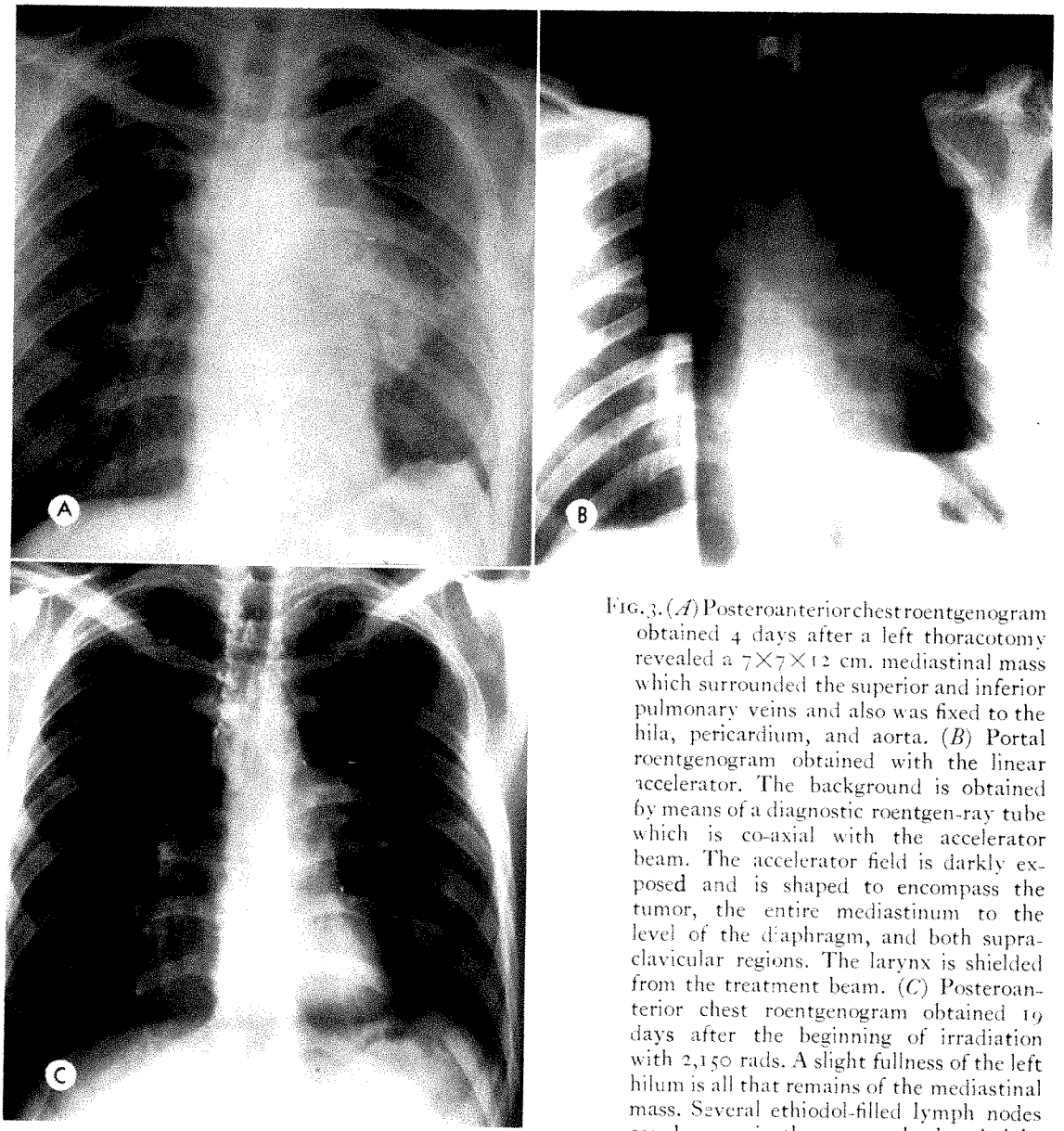


FIG. 3. (*A*) Posteroanterior chest roentgenogram obtained 4 days after a left thoracotomy revealed a 7×7×12 cm. mediastinal mass which surrounded the superior and inferior pulmonary veins and also was fixed to the hila, pericardium, and aorta. (*B*) Portal roentgenogram obtained with the linear accelerator. The background is obtained by means of a diagnostic roentgen-ray tube which is co-axial with the accelerator beam. The accelerator field is darkly exposed and is shaped to encompass the tumor, the entire mediastinum to the level of the diaphragm, and both supraclavicular regions. The larynx is shielded from the treatment beam. (*C*) Posteroanterior chest roentgenogram obtained 19 days after the beginning of irradiation with 2,150 rads. A slight fullness of the left hilum is all that remains of the mediastinal mass. Several ethiodol-filled lymph nodes can be seen in the paratracheal and right supraclavicular regions. Patient received a total dose of 3,950 rads in 32 days and is living and well at 6 years and 4 months.

tity. The treated volume should be liberal and should include the entire mediastinum and supraclavicular region (Fig. 3, *A*, *B* and *C*). The response of the neoplasm should be closely monitored with frequent chest roentgenograms, since dramatic response is so common that the heart and pericardium may be spared unnecessary irradiation by progressive shrinkage of the treated volume.

As with seminoma testis, metastatic spread does not negate the possibility of cure. A roentgen skeletal survey and abdominal lymphangiography should be performed in order to detect unusual metastatic sites. Metastases should be irradiated aggressively with the intention of sterilizing the neoplasm. Long survival has been reported in several instances after radiation therapy of multiple sites.

Although cures have been achieved by surgery alone, frequently the neoplasm is large when discovered and aggressively invades nonresectable mediastinal structures. In view of the modest dose of radiation required for adequate lethal effect on the tumor cells, a subtotal surgical removal seems of little value, and in fact, may disseminate the neoplasm beyond the reach of adequate irradiation. A relatively restricted but adequate biopsy with minimum manipulation of the tissues is a more appealing prelude to definitive radiation therapy. In less advanced cases in which gross total surgical removal can be performed, it seems reasonable to follow surgical resection with radiation therapy in every instance.

SUMMARY AND CONCLUSIONS

1. Primary mediastinal seminoma, although of obscure origin, appears to be a distinctive clinical entity.

2. It is infrequently cured by resection only.

3. Like seminoma testis, it is both radiosensitive and radiocurable.

4. Lymphangiography should be employed for evaluation of possible paraaortic metastases.

5. Whether or not totally resected, the mediastinum and supraclavicular lymph nodes should be irradiated *en bloc*.

6. A tumor dose of 4,000–4,500 rads in 4 weeks appears to be adequate.

7. Subsequent metastases, though multiple, should be vigorously pursued and irradiated to the same tumor dose.

Malcolm A. Bagshaw, M.D.
Division of Radiation Therapy
Stanford Medical Center
Palo Alto, California 94304

REFERENCES

1. Audier, M., Dor, J., Picard, D., Payan, H., Clement, G. L., and Galinier, L. Thymoma "pseudo-seminoma." *Presse méd.*, 1960, *68*, 574–576.
2. Azzopardi, J. G., Mostofi, F. K., and Theiss, E. A. Lesions of testes observed in certain patients with widespread choriocarcinoma and related tumors. *Am. J. Path.*, 1961, *38*, 207–225.
3. Effler, D. B., and McCormack, L. J. Thymic neoplasms. *J. Thoracic Surg.*, 1956, *31*, 60–82.
4. Friedman, N. B. Comparative morphogenesis of extragenital and gonadal teratoid tumors. *Cancer*, 1951, *4*, 265–276.
5. Ginzton, E. L., Mallory, K. B., and Kaplan, H. S. Stanford medical linear accelerator. I. Design and development. *Stanford M. Bull.*, 1957, *15*, 123–140.
6. Inada, K., and Nakano, A. Germinoma of mediastinum: case report with special reference to histogenesis of mediastinal teratoma. *Dis. Chest*, 1959, *36*, 438–441.
7. Inada, K., Kawasaki, A., and Hamazaki, M. Germinoma of mediastinum: critical review of classification of thymic neoplasms. *Am. Rev. Resp. Dis.*, 1963, *87*, 560–567.
8. Kaplan, H. S., and Bagshaw, M. A. Stanford medical linear accelerator. III. Application to clinical problems of radiation therapy. *Stanford M. Bull.*, 1957, *15*, 141–151.
9. Kaplan, H. S., and Rosenberg, S. A. Extended-field radical radiotherapy in advanced Hodgkin's disease: short-term results of 2 randomized clinical trials. *Cancer Res.*, 1966, *26*, 1268–1276.
10. Kleitsch, W. P., Taricco, A., and Haslam, G. J. Primary seminoma (germinoma) of mediastinum. *Ann. Thorac. Surg.*, 1967, *4*, 249–255.
11. Kountz, S. L., Connolly, J. E., and Cohn, R. Seminoma-like (or seminomatous) tumors of anterior mediastinum: report of four new cases and review of literature. *J. Thoracic & Cardiovasc. Surg.*, 1963, *45*, 289–301.
12. Kuznetsov, I. D., Lavnikova, G. A., and Koroleva, O. F. Two cases of seminoma of mediastinum. *Vop. Onkol.*, 1961, *7*, 55–61.
13. Lattes, R. Thymoma and other tumors of thymus: analysis of 107 cases. *Cancer*, 1962, *15*, 1224–1260.
14. Molina, C., Mercier, R., DeLage, J., de Lagvillamie, B., and Cheminat, J. C. Les séminomes du médiastin. *Sem. Hôp. Paris*, 1965, *41*, 1416–1423.
15. Nazari, A., and Gagnon, E. D. Seminoma-like tumor of mediastinum: case report. *J. Thoracic & Cardiovasc. Surg.*, 1966, *51*, 751–754.
16. Oberman, H. A., and Libcke, J. H. Malignant germinal neoplasms of mediastinum. *Cancer*, 1964, *17*, 498–507.
17. O'Gara, R. W., Horn, R. C., Jr., and Enterline, H. T. Tumors of anterior mediastinum. *Cancer*, 1958, *11*, 562–590.
18. Pachter, M. R., and Lattes, R. Germinal tumors of mediastinum: clinicopathologic study of adult teratomas, teratocarcinomas, choriocarcinomas and seminomas. *Dis. Chest*, 1964, *45*, 301–310.
19. Pugsley, W. S., and Carleton, R. L. Germinal nature of teratoid tumors of thymus. *A.M.A. Arch. Path.*, 1953, *56*, 341–347.

20. RATHER, L. J., GARDINER, W. R., and FRERICKS, J. B. Regression and maturation of primary testicular tumors with progressive growth of metastases: report of six new cases and review of literature. *Stanford M. Bull.*, 1954, *12*, 12–25.
21. ROBINSON, B. W. Germinal neoplasia of extragenital origin. *J. Nat. M. A.*, 1960, *52*, 162–165.
22. SCHLUMBERGER, H. G. Teratoma of anterior mediastinum in group of military age: study of 16 cases and review of theories of genesis. *Arch. Path.*, 1946, *41*, 398–444.
23. SCHLUMBERGER, H. G. Tumors of mediastinum. In: Atlas of Tumor Pathology. Sect. V, Fasc. 18, Armed Forces Institute of Pathology, Washington, D. C., 1951.
24. STEINMETZ, W. H., and HAYS, R. A. Primary seminoma of mediastinum: report of case with unusual site of metastasis and review of literature. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1961, *86*, 669–672.
25. STEWART, J. R., COHN, K. E., FAJARDO, L. F., HANCOCK, E. W., and KAPLAN, H. S. Radiation-induced heart disease: study of twenty-five patients. *Radiology*, 1967, *89*, 302–310.
26. TANIGUCHI, H., PAI, T. J., and AMDKATA, Y. Two cases of seminomatous tumors originating from anterior mediastinum. *Gann*, 1957, *48*, 639–641.
27. WOOLNER, L. B., JAMPLIS, R. W., and KIRKLIN, J. W. Seminoma (germinoma) apparently primary in anterior mediastinum. *New England J. Med.*, 1955, *252*, 653–657.

Vol. 105, No. 1

ANGIOGRAPHIC MANIFESTATIONS OF WILMS' TUMOR*

AN OBSERVATION OF SIX CASES

By CHIEN-HSING MENG, M.D., *and* MILTON ELKIN, M.D.
BRONX, NEW YORK

THE important role of angiography in the diagnosis of renal carcinoma is well established. However, the angiographic study of Wilms' tumor (nephroblastoma) is not general practice.[6,8] This is probably due to the belief that the diagnosis of a Wilms' tumor can be made on clinical grounds and with the more commonly performed examination of intravenous urography. Also because of the accepted, although not conclusively proved, view that immediate surgery is the treatment of choice for patients with this neoplasm, unnecessary handling and sophisticated preoperative investigations are considered by some investigators to be contraindicated.

Whereas Wilms' tumor is managed in most centers by immediate operation, in some institutions radiation therapy and sometimes chemotherapy are administered before surgery. In the presence of an abdominal mass without visualization of the ipsilateral calyceal system on urography, misdiagnosis and incorrect management can occur. Occasionally there is the problem of differentiating a neuroblastoma of the adrenal gland invading the kidney from a Wilms' tumor extending beyond the kidney. When a Wilms' tumor occurs in a horseshoe or an ectopic kidney, the urographic diagnosis may be extremely difficult.[1] Hence, if renal angiography can be of help in establishing the correct diagnosis in the questionable cases, or providing accurate preoperative information in the usual cases, its performance seems justified and worthwhile.

There have been only scattered references to the use of angiography in Wilms' tumor.[2-6] Recently, McDonald and Hiller[4] published probably the largest series of cases studied with angiography. Inferior cavography was done in 11 of their 12 patients and 7 were subjected to aortography. Their experience indicated that angiography can be done without difficulty, delay or undue hazard while providing useful information for planned and more specific treatment of malignant disease in childhood. They concluded that the diagnosis of Wilms' tumor can be made on aortography alone with the findings of florid tumor circulation and the replacement of renal substance by tumor tissue. Farah and Lofstrom,[2] in presenting 2 other cases of Wilms' tumor, even suggested the presence of a peculiar and specific angiographic pattern in this neoplasm. However, Olsson[5] stated that renal angiography of the few cases examined by him showed essentially the same features as those of renal carcinoma.

It is the purpose of the authors to report their experience of angiography in Wilms' tumor and to review the angiographic manifestations as observed in a series of 6 patients.

MATERIAL AND METHOD

In the past few years we have had the opportunity of performing angiographic study on 6 patients with nephroblastoma. There is 1 case of adult Wilms' tumor; the other 5 are in the pediatric age group below 6 years.

In the children the examination was done after heavy sedation as well as local anesthesia. Cutdown of the femoral artery had to be performed in a 9 month old child.

* From the Department of Radiology, Albert Einstein College of Medicine, Yeshiva University and Bronx Municipal Hospital Center, Bronx, New York.
Supported in part by Grant 5M01-FR66-0G51 RISI of the National Institutes of Health (General Clinical Research Center-Acute).

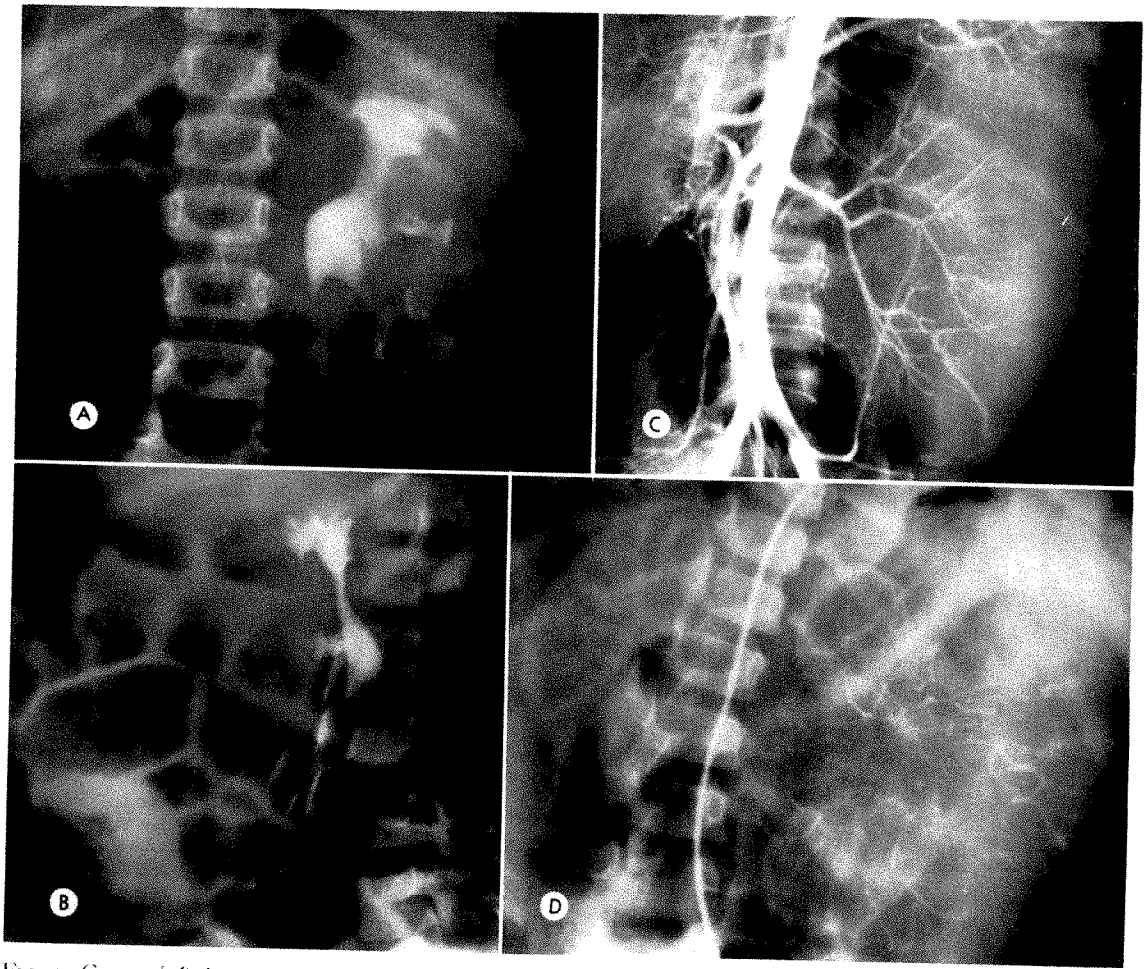


FIG. 1. Case 1. (*A*) Anteroposterior intravenous urogram demonstrates general enlargement of the left kidney with a distorted megacalyceal system. (*B*) Lateral urogram demonstrates anterior location of the tumor mass with the left calyceal system displaced and distorted. (*C*) Anteroposterior aortogram shows contralateral displacement of the aorta, marked splaying and stretching of the intrarenal arterial branches. (*D*) Aortogram (nephrographic phase) shows prominent, scattered tumor vessels without arteriovenous shunting.

In the other 5 patients a percutaneous transfemoral (Seldinger) technique was used. In the 3 earlier cases only aortography was done; in the other 3 patients both aortography and selective angiography were performed. Standard practice of the angiographic procedure with image intensifier monitoring and rapid serial filming was followed.

REPORT OF CASES

CASE 1. A. D., a 4 year old boy, presented with asymptomatic abdominal swelling of 1 year's duration. Physical examination revealed a large, firm, left abdominal mass. Intravenous urography (Fig. 1*A*) showed a huge left kidney with an enlarged, moderately distorted calyceal system especially in its cephalad portion. The lateral projection (Fig. 1*B*) demonstrated the mass to be primarily in the anterior aspect of the kidney displacing the pelvis and calyces posteriorly. The right kidney appeared normal. Aortography (Fig. 1, *C* and *D*) revealed displacement of the aorta to the right by the large left flank mass which extended from the level of the dome of the diaphragm to the iliac crest. The mass was supplied by the renal artery with stretching and splaying of its branches. The left main renal artery was of

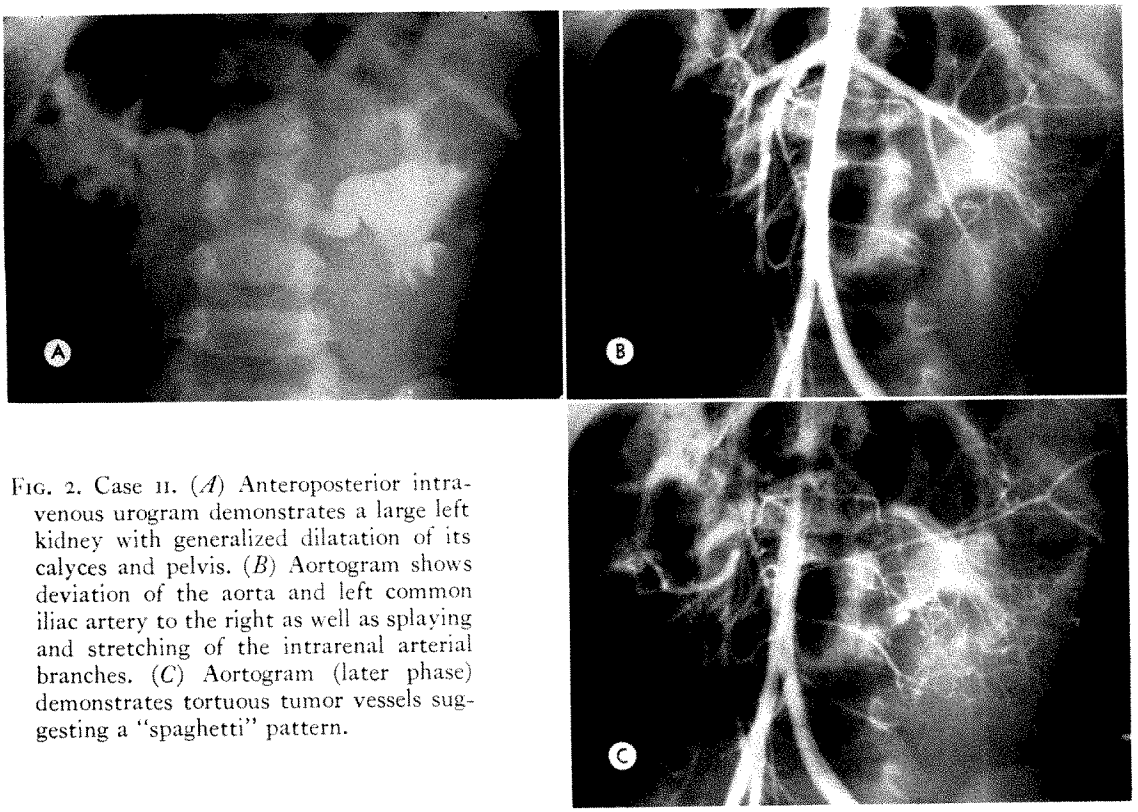


Fig. 2. Case II. (*A*) Anteroposterior intravenous urogram demonstrates a large left kidney with generalized dilatation of its calyces and pelvis. (*B*) Aortogram shows deviation of the aorta and left common iliac artery to the right as well as splaying and stretching of the intrarenal arterial branches. (*C*) Aortogram (later phase) demonstrates tortuous tumor vessels suggesting a "spaghetti" pattern.

normal caliber. Prominent and tortuous tumor vessels were demonstrated, especially in the later phase of the angiogram; some of these vessels were abnormal draining veins.

Telecobalt therapy was started but had to be discontinued before completion of the planned course because of evidence of bleeding into the tumor. A tumor dose of 350 r had been delivered. Emergent exploration was performed and the left kidney harboring the huge tumor was removed. The tumor was well encapsulated with no evidence of extension beyond the kidney. Postoperatively the patient received a 5 day course of actinomycin D. He has remained well for 3 years.

Case II. P. M., a 5 year old boy, entered the hospital because of a large abdominal mass noted by his mother on the day of admission. On physical examination there was a firm left abdominal mass about 7 cm. in diameter. There was also a left varicocele. Intravenous urography (Fig. 2*A*) showed a large left kidney and large pelvicalyceal system with no localized deformity of the calyces. The right kidney appeared normal. Aortography (Fig. 2, *B* and *C*) demonstrated deviation of the aorta and the left common iliac artery to the right. The left renal artery was elongated, yet of normal caliber, with stretching and splaying of its branches. There were numerous tortuous and irregular (tumor) vessels in the huge renal mass, especially in its midportion and lower pole. Several of the left lumbar vessels in the region of the mass appeared enlarged and possibly contributed to the tumor's vascularity.

The patient received preoperative irradiation to a total tumor dose of 1,200 r in 15 treatment days. At surgery the tumor was found to have extended beyond the renal capsule with involvement of the descending colon. There was extensive perirenal venous enlargement. Left nephrectomy and segmental resection of the colon were performed. The surgical specimen presented as a 12×5×5 cm. yellowish-brown tumor mass with areas of hemorrhage and cystic degeneration.

Postoperatively, the patient received additional irradiation (1,260 r tumor dose in 16 days) in combination with one course of actinomycin D. In the next 6 months there was increasing evidence of widespread metastases to

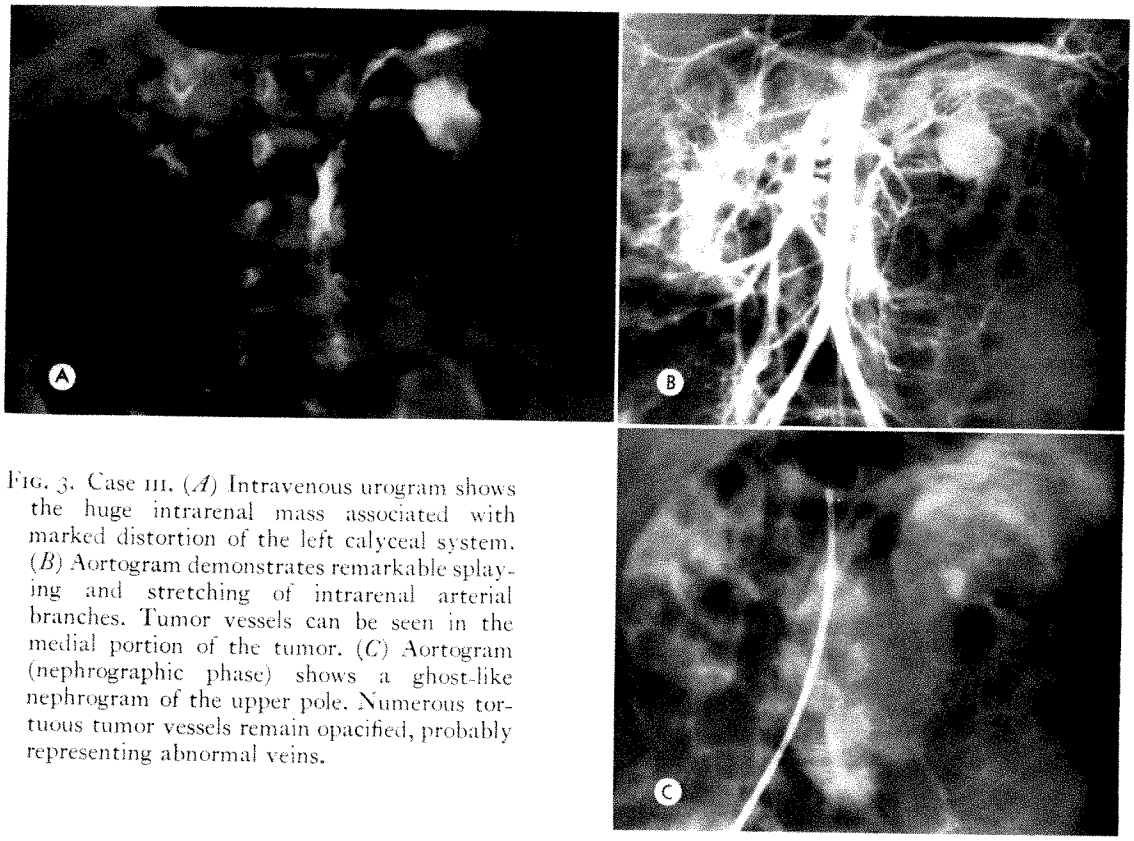


FIG. 3. Case III. (*A*) Intravenous urogram shows the huge intrarenal mass associated with marked distortion of the left calyceal system. (*B*) Aortogram demonstrates remarkable splaying and stretching of intrarenal arterial branches. Tumor vessels can be seen in the medial portion of the tumor. (*C*) Aortogram (nephrographic phase) shows a ghost-like nephrogram of the upper pole. Numerous tortuous tumor vessels remain opacified, probably representing abnormal veins.

lungs, skull and other bones. The patient died 9½ months after the initial hospital admission.

CASE III. M. M., a 9 month old girl was admitted to the hospital for treatment of a respiratory infection. Physical examination disclosed a large left upper quadrant mass. Urine examination was normal. Intravenous urography (Fig. 3*A*) showed a large mass occupying the lower aspect of the left kidney with distortion of the pelvicalyceal system. The renal pelvis was displaced toward the right and the opacified infundibula were stretched with dilatation of the visualized calyces. The right kidney appeared normal. Aortography (Fig. 3*B*) showed the left renal artery to be displaced

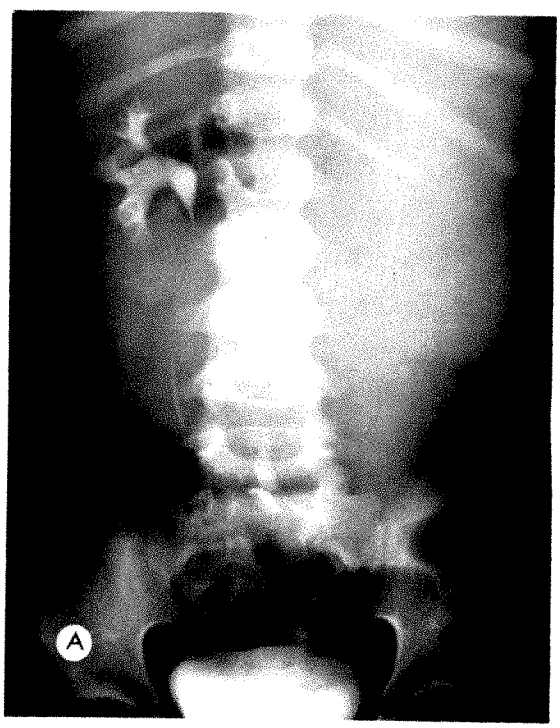


FIG. 4. Case IV. (*A*) Intravenous urogram shows a large abdominal tumor associated with downward displacement and distortion of the left calyceal system.

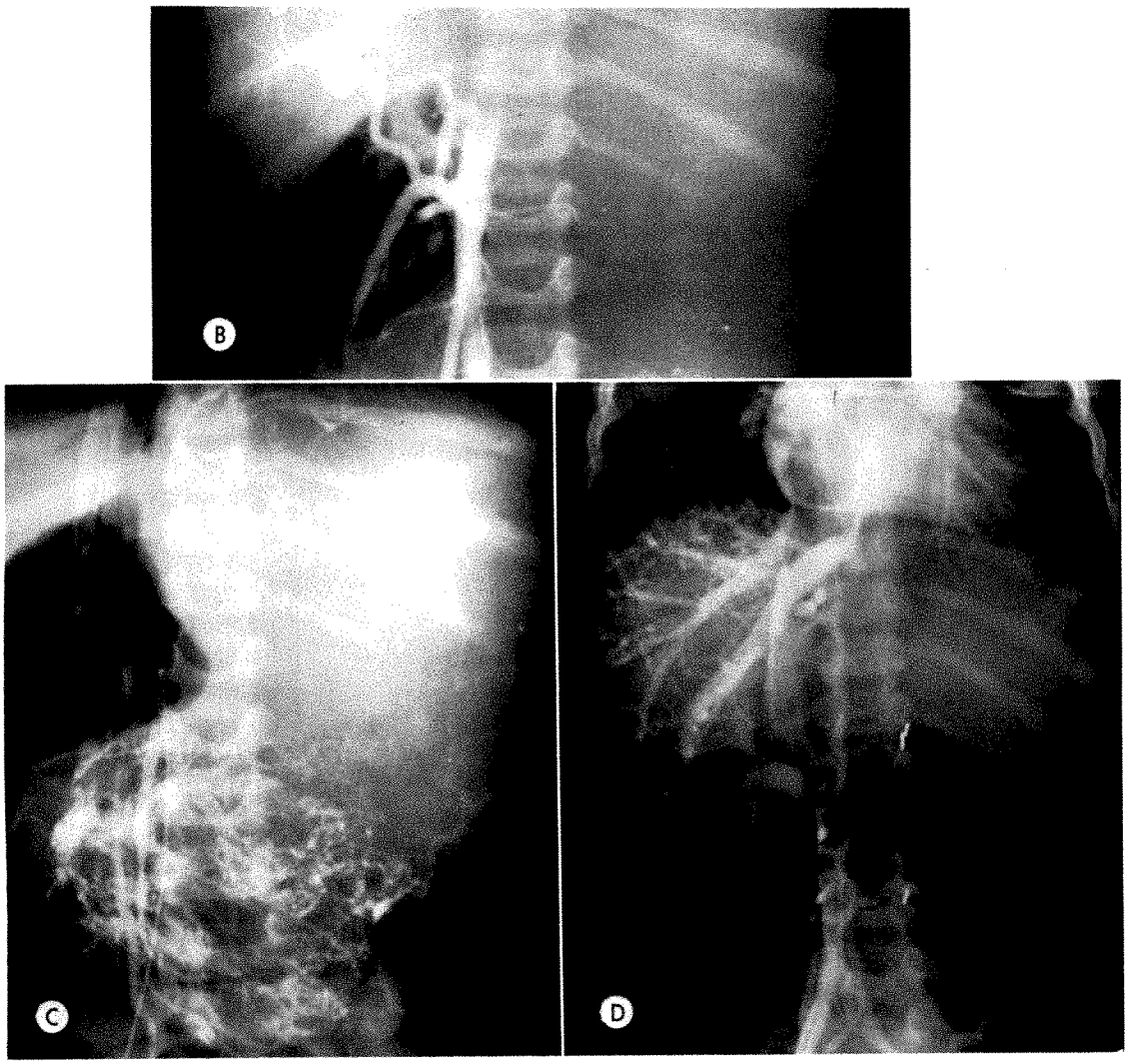


Fig. 4. (*B*) Aortogram demonstrates contralateral displacement of the aorta. The left renal artery is larger than the right, elongated and stretched downward. (*C*) Selective left renal angiogram shows extensive tumor vessels in the lower half of the tumor. Large avascular area is seen in the upper half with a few tumor vessels at its upper periphery. The inferior vena cava presents immediate opacification with numerous linear filling defects. (*D*) Postoperative cavography shows large tumor thrombi in the vena cava and the right atrium of the heart.

cephalad with stretching of its branches as well as irregularity of some of the branches. The lower half of the left kidney was completely replaced by the tumor. The irregular, tortuous tumor vessels were especially well demonstrated in the later phase of the aortogram (Fig. 3*C*).

The patient received irradiation, 1,000 r tumor dose in a 15 day period, with shrinking of the mass to about two-thirds of its original size. Left nephrectomy was then done. A lobulated oval mass, measuring 3.5×3×2.5 cm. and covered by a thin capsule, occupied the lower half of the kidney. The yellowish-white tumor was of rubbery consistency with several areas of degeneration. Postoperatively the patient was given a course of actinomycin D. At a 6 month follow-up examination she was doing well. The patient returned to Puerto Rico and further follow-up is not available.

Case iv. J. B., a 5 year old girl, suddenly developed loss of appetite and severe listlessness 2 weeks prior to hospital entry. An abdominal

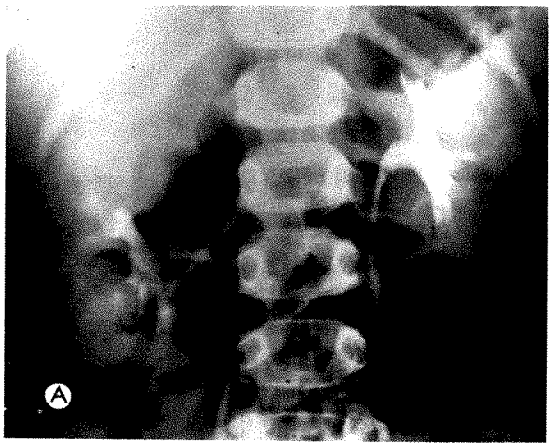


FIG. 5. Case v. (*A*) Intravenous urogram reveals tilting of the right renal axis suggesting the presence of an upper pole mass.

mass was noted by the mother for the first time 3 days before admission. Intravenous urography (Fig. 4*A*) showed the huge mass to fill the left abdomen and to extend across the midline with lateral displacement of the right ureter. The distorted calyceal system of the left kidney was displaced markedly caudad, being located at the level of L-5 and the upper sacrum close to the midline. The right kidney appeared normal. Aortography (Fig. 4*B*) showed displacement of the aorta to the right. The left renal artery was directed downward, being pushed markedly to the right; its caliber was enlarged. Selective left renal angiography (Fig. 4*C*) demonstrated extensive tumor vasculature in the lower part of the mass with a few tumor vessels at its upper periphery. There was immediate opacification of the inferior vena cava, indicating an arteriovenous shunting in the tumor, although no well-defined renal vein could be identified.

At surgery the tumor was found to be so massive that only a subtotal excision was done. The tumor extended into the renal vein and up into the inferior vena cava. A postoperative cavography (Fig. 4*D*) demonstrated tumor filling the upper half of the inferior vena cava with extension into the right atrium. Postoperative irradiation (3,000 r tumor dose in 4 weeks) and a course of actinomycin D were administered. The patient died 6 months after surgery.

Autopsy disclosed widespread metastases to the inferior vena cava, hepatic veins, right atrium of the heart, portal veins, right lung and peritoneum.

CASE V. W. N., a 5½ year old girl, was admitted to the hospital with chills, fever and urinary frequency. She developed right-sided abdominal pain and the diagnosis of acute appendicitis was considered. Urinary examination revealed a few red blood cells and white blood cells. There was no abdominal mass palpable. Intravenous urography (Fig. 5*A*) showed a mass in the medial aspect of the upper pole of the right kidney, displacing the kidney downward and tilting its upper pole laterally. The calyces and pelvis were not distorted. The left kidney appeared normal. Aortography (Fig. 5*B*) showed the right renal artery to be elongated but of normal caliber. A relative lack of vessels was noted at the upper pole of the right kidney. Selective right renal angiography (Fig. 5, *C* and *D*) revealed hypovascularity of the mass with diminution of the nephrogram intensity in that area. Among the diagnoses entertained was renal abscess. However, tortuous abnormal vessels were seen within the mass, especially at the late stage of the angiogram.

Right nephrectomy was done. The tumor was cystic with areas of hemorrhage in the tumor as well as a small retroperitoneal hematoma. Postoperative irradiation (3,000 r in 3 weeks) and a 5 day course of actinomycin D were administered. So far, in a follow-up period of 11 months, the patient is doing well.

CASE VI. K. F., a 43 year old woman, presented with weakness and weight loss of 4 weeks' duration. Physical examination disclosed a nontender, firm, oval, mobile mass in the left upper quadrant, measuring 15×20 cm. Urine examination showed 10–20 white blood cells per high powered field. Intravenous urography (Fig. 6*A*) revealed the large mass to occupy the upper portion of the left kidney with downward and medial displacement of the distorted calyceal system. Mottled small calcification densities were scattered in several areas of the mass. The right kidney appeared normal. The aortogram (Fig. 6*B*) showed deviation of the aorta to the right. The left renal artery was markedly stretched, relatively narrow in caliber and displaced caudally. An upper left lumbar artery pursued an irregular course and appeared to supply part of the tumor. The splenic artery was displaced cepha-

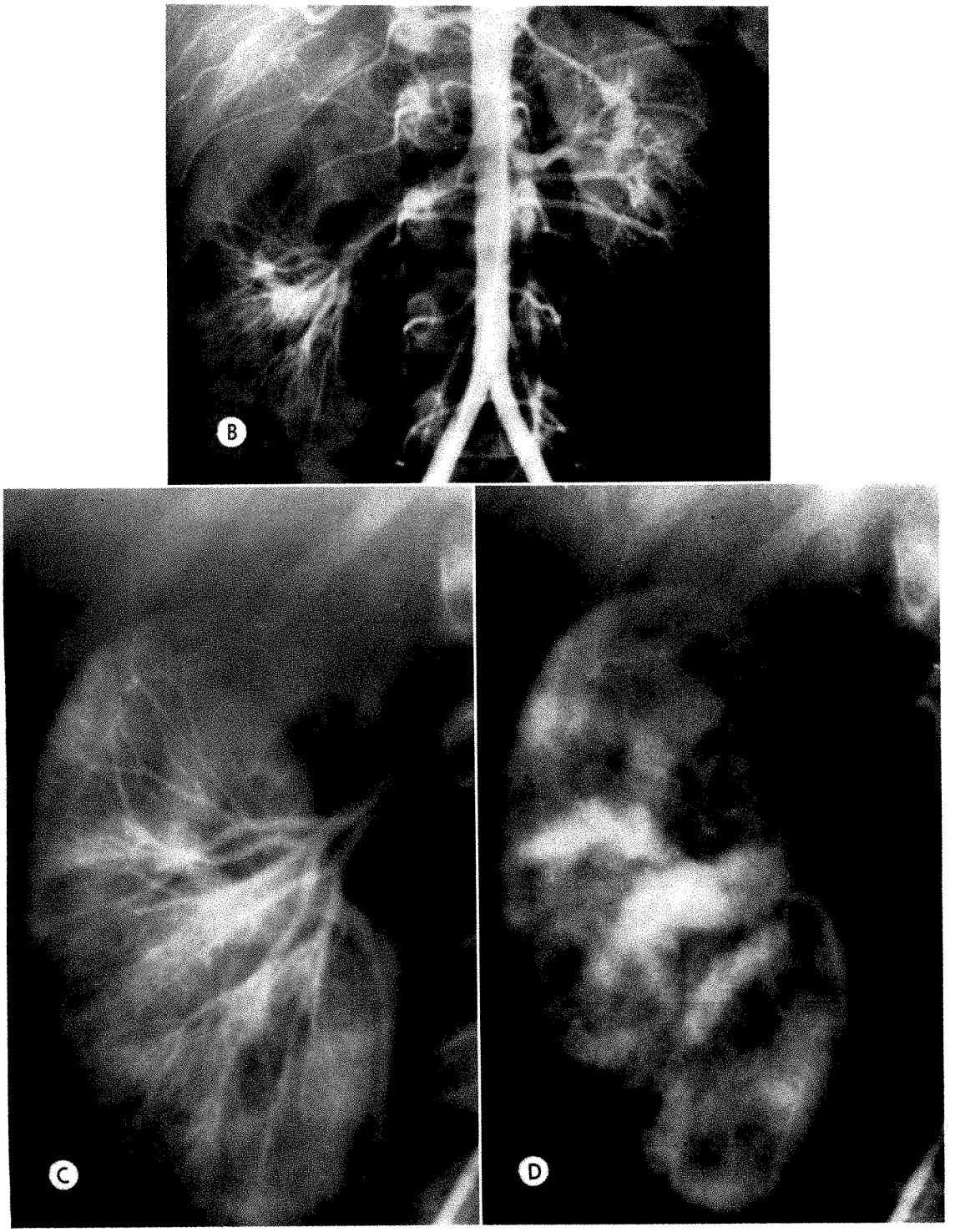


FIG. 5. (*B*) Aortogram shows elongation of the right renal artery. The upper pole appears relatively hypovascular. (*C*) Selective right renal angiogram shows splaying of the arterial branches to the upper pole. (*D*) Selective right renal angiogram (nephrographic phase) demonstrates a few tumor vessels at the periphery of the tumor.

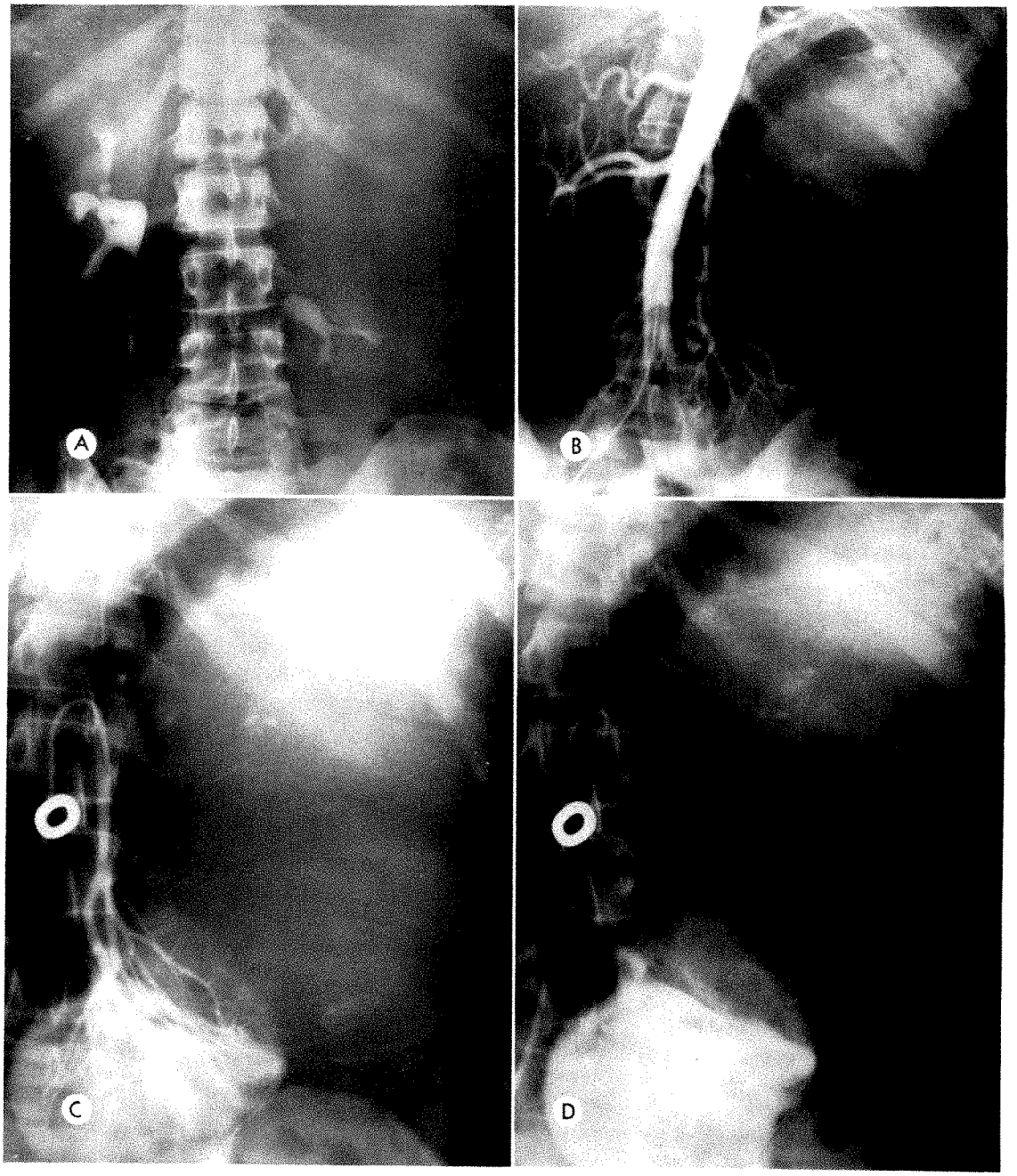


FIG. 6. Case VI. (*A*) Intravenous urogram shows a large mass in the left kidney with downward displacement of the calyceal system. Small calcific densities are seen scattered in the superior and medial aspects of the mass. (*B*) Aortogram demonstrates deviation of the aorta as well as displacement and downward stretching of the left renal artery. The splenic artery is displaced cephalad. (*C* and *D*) Selective left renal angiograms show several small clusters of tumor vessels and tumor stain in the inferior portion of the mass although most of the mass is avascular. The remaining portion of the left kidney shows a normal nephrogram.

lad. Selective left renal angiography (Fig. 6, *C* and *D*) showed crowding of the renal artery branches with several small clusters of tumor vessels and tumor stain in the inferior portion of the mass. In general, however, the tumor was hypovascular.

Left nephrectomy was done. The mass measured 15×13×6 cm. with a normal-appearing portion of the left kidney at the lower pole of the mass. The brownish-yellow tumor, encapsulated by a thin layer of fibrous tissue, was of firm consistency with large areas of cystic degeneration.

Within a few months of surgery the patient developed pulmonary metastases and pleural fluid and died.

DISCUSSION

In the 6 patients in our series, the tumor was located in the left kidney in 5 of them. As is common with Wilms' tumor the mass was large in all our cases at the time of discovery. Displacement of the aorta was seen in 4 patients with huge left-sided tumors. The renal artery to the involved kidney was of increased diameter in 1 patient, decreased diameter in 1 patient and about of normal caliber in the remaining 4 patients. Elongation of the renal artery was present in all 6 patients, markedly so in 3; splaying and stretching of the arterial branches were seen in all 6. This finding, of course, is related to the mass of the tumor. Abnormal ("tumor") vessels were demonstrated in all 6 patients—sparingly in 2, moderately in 3, and extensively in 1.

The type of tumor vasculature is not pathognomonic, although in general these 6 cases showed what might be described as a "creeping vine" or "spaghetti" pattern. Puddling of contrast medium was not a feature of these tumors and scattered small areas of tumor stain were seen in only 1 patient (Case VI). In general the vessels in the tumor were discrete, pursuing a tortuous course over long lengths, of irregular diameters but in general of large caliber throughout their visualized course. The smudging of vessel outline seen so commonly in renal cell carcinoma was not a feature of our patients with Wilms' tumor. The late arterial and nephrographic phases of the angiogram showed the abnormal vasculature to its best extent. Arteriovenous shunting with immediate opacification of the inferior vena cava was seen in only Case IV.

All our cases showed avascular areas of varying size within the tumor mass. In the nephrographic phase the avascular component appeared as ill-defined and irregular as areas of relative radiolucency. In general, the nephrogram intensity was reduced on the side of involvement, although in Cases V and VI there was a nephrogram of normal intensity in the unaffected portion of the kidney. This, of course, is an index of the extent of kidney destroyed by the tumor.

SUMMARY

Angiographic study was made in 6 patients with Wilms' tumor, 5 children and 1 adult. In all cases tumor vessels could be demonstrated—moderately vascular in 3, hypovascular in 2, and markedly vascular in 1. Tumor stain was demonstrated in only 1 patient, and then in only a few small scattered areas. The tumor vessels in these 6 patients had a "creeping vine" or "spaghetti" appearance. There were avascular areas of varying size within the tumor mass in all 6 cases.

The type of abnormal vascularity might suggest the diagnosis of Wilms' tumor although it is not proposed to be pathognomonic of this type of neoplasm.

Chien-Hsing Meng, M.D.
Department of Radiology
Albert Einstein College of Medicine
Yeshiva University
1300 Morris Park Avenue
Bronx, New York 10461

REFERENCES

1. Caffey, J. Pediatric X-ray Diagnosis: A Textbook for Students and Practitioners of Pediatrics, Surgery, and Radiology. Fifth edition. Year Book Medical Publishers, Chicago, 1967, p. 664.
2. Farah, J., and Lofstrom, J. E. Angiography of Wilms' tumor. *Radiology*, 1968, *90*, 775–777.
3. Hope, J. W., and Borns, P. F. Radiologic diagnosis of primary and metastatic cancer in infants and children. *Radiol. Clin. North America*, 1965, *3*, 353–374.
4. McDonald, P., and Hiller, H. G. Angiography

in abdominal tumors in childhood with particular reference to neuroblastoma and Wilms' tumor. *Clin. Radiol.*, 1968, *19*, 1–18.
5. OLSSON, O. Diagnostic Radiology. In: Handbook of Urology. Volume V. Edited by C. E. Alken, V. W. Dix, H. M. Weyrauch, and E. Wildbolz. Springer-Verlag, Berlin, 1962, p. 194.
6. SUSSMAN, M. L., JACOBSON, G., and JAYNE, E. H. Urologic Roentgenology. Williams & Wilkins Company, Baltimore, 1967, p. 8.202.
7. SUTTON, D. Arteriography. E. & S. Livingstone, Ltd., London, 1962, p. 137.
8. WILLIAMS, D. I. Nephroblastoma: clinical picture and diagnosis. In: Tumours of the Kidney and Ureter. Edited by E. Riches. Williams & Wilkins Company, Baltimore, 1964.

SURGICAL MANAGEMENT OF SOLID TUMORS IN CHILDHOOD*

By LESTER W. MARTIN, M.D.†
CINCINNATI, OHIO

SOLID soft-tissue tumors of childhood are best managed by a team consisting of a pediatrician, a radiologist, a chemotherapist, a pathologist and a surgeon. The ideal treatment of any solid tumor is complete surgical removal prior to metastatic spread. Unfortunately, in many instances, the tumor has already undergone metastasis before medical help is sought. In either instance, it is important that the entire team be involved in the care of the child.

WILMS' TUMOR

In our experience, complete surgical removal has been possible in every case of Wilms' tumor if metastasis has not occurred. The Wilms' tumor remains encapsulated for a long period of time and may reach enormous size prior to erosion through the capsule, direct invasion of adjacent organs, or metastatic spread to local lymph nodes or to the lungs. In this report, which involves over 50 patients with Wilms' tumor, size has been no contraindication to surgical removal. An unusually large tumor presents an exciting challenge to the experienced surgeon, yielding results which are particularly gratifying (Fig. 1).

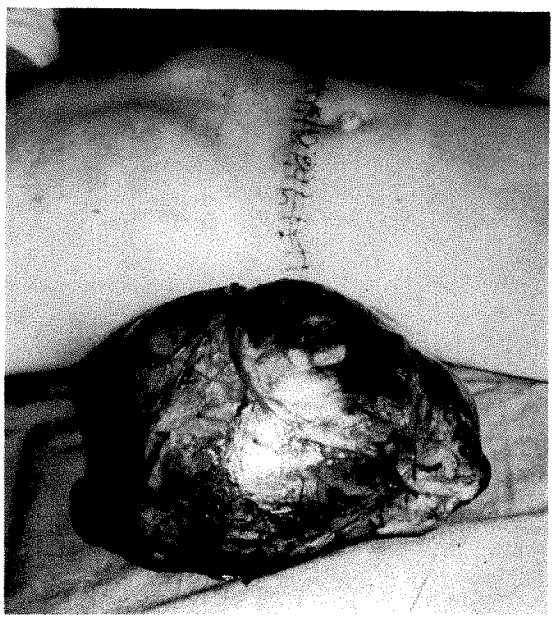


FIG. 1. An unusually large Wilms' tumor of the right kidney was removed with relative ease since it arose from the posterior aspect of the kidney displacing the renal vessels forward. The patient is living and well 7 years later.

The position of the tumor within the kidney pelvis is of more significance than the size in regard to surgical removal. If the tumor arises from the lower pole of the kidney, displacing the renal pelvis upward, the renal pedicle may be displaced far up beneath the costal margin and surgical exposure may be more adequately provided through a thoraco-abdominal type of incision. A tumor arising from the posterior aspect of the kidney will displace the renal pedicle forward, and, even though the tumor is extremely large, the renal vessels are long and readily exposed through an abdominal approach. If the tumor arises directly opposite the renal pedicle displacing the kidney medially, the pedicle may be shortened, thereby creating a more difficult situation for the surgeon. We have preferred a transverse abdominal incision extending from flank to flank except when a thoraco-abdominal approach is required, in which case, one end of the incision is placed higher to include the thoracic cage. At the time of operation an effort is made to ligate the renal pedicle as early in the course of the operation as possible. In the last 38 patients with Wilms' tumor whom we have operated upon, a sample of blood has been

* Presented at the Fiftieth Annual Meeting of the American Radium Society, Miami Beach, Florida, April 7–11, 1968.
† Associate Professor of Surgery, The College of Medicine, University of Cincinnati; and Director of Pediatric Surgery, The Children's Hospital, Cincinnati, Ohio.

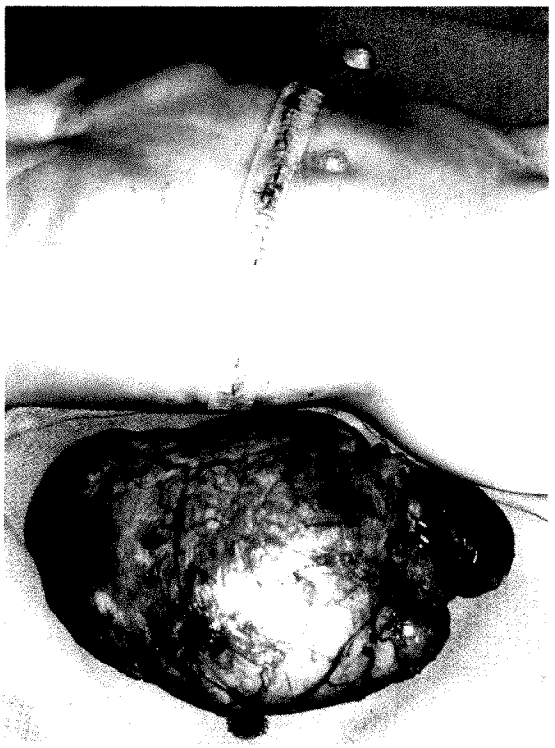


FIG. 2. This child had bilateral Wilms' tumors. The small tumor of the left kidney was unsuspected prior to operation and since it arose from the posterior aspect of the kidney, was found only after complete mobilization and careful inspection of the organ.

drawn from the renal vein prior to its ligation and again following removal of the tumor—the second blood sample being drawn from the tumor side of the renal vein. Tumor cells have been identified rarely in the initial specimen, but frequently in the second specimen, indicating the effect of surgical manipulation upon the dissemination of tumor cells into the blood stream, and indicating the necessity for early ligation of the renal pedicle in the course of the operation. This finding has also led us to the strong conviction that something should be placed in the bloodstream to hinder implantation of the circulating tumor cells. Our routine has included an intravenous injection of Actinomycin D during the operation as soon as the diagnosis has been established with reasonable certainty, and after the surgeon has indicated his confidence that the tumor can be removed without undue blood loss or other systemic effect on the patient.

Since approximately 10 per cent of Wilms' tumors are bilateral,[2] it is our feeling that the opposite kidney should routinely be examined by direct vision as well as by palpation. An examination should be made of both the anterior and posterior aspects of the kidney in a search for a primary tumor on the opposite side. The child in Figure 2 was found unexpectedly at operation to have a small tumor involving the posterior aspect of the opposite kidney. This particular tumor would have been overlooked if the kidney had been examined only by the palpating hand of the surgeon passing over the front of the kidney.

A retroperitoneal lymph node dissection, removing carefully any retroperitoneal tissues which may harbor metastatic disease in the regional lymph nodes, has been carried out routinely in our patients for the past 10 years. We have 2 children living 3 years and 7 years in whom the pathologist reported metastatic disease to the regional lymph nodes, removed at the time of operation.

Radiation therapy has been initiated immediately following operation in all of our patients except those in the neonatal period. This has been carried out in conjunction with systemic Actinomycin D therapy. We have not utilized preoperative irradiation for the following reasons: (1) with modern surgical techniques, it is no longer necessary to reduce the size of the tumor in order to remove it; (2) the preoperative diagnosis cannot be established with certainty, and, consequently, a benign lesion may be treated with unnecessary or even harmful irradiation; and (3) dissemination of tumor cells may result from the inevitable handling of the child and repeated palpation of the tumor during the extended preoperative hospital stay.[3]

Pulmonary metastasis is an ominous sign but it does not necessarily indicate a fatal prognosis. Radiation therapy to the involved lung combined with systemic Actinomycin D has resulted in several longterm

survivals. There are also several documented cases of longterm survival following surgical resection of individual metastatic pulmonary lesions. It is our feeling that resection is indicated for individual lesions which recur or persist following Actinomycin D and roentgen therapy. As small an amount of pulmonary tissue as possible should be removed with the metastatic lesion. We have one child who has undergone 5 separate pulmonary resections for metastasis. The last resection was over 5 years ago. She is well and free of any evidence of disease at the present time.

The neonate with a Wilms' tumor has been considered a somewhat different and a purely surgical problem. The tumor, along with the kidney and the adjacent retroperitoneal lymph nodes, are all removed. We have not employed chemotherapy or radiation therapy for the neonate.

The inferior vena cavagram has been found to be of limited value to the surgeon. Direct invasion of the vena cava may not be demonstrable roentgenographically, and apparent complete obstruction may be a result of extrinsic compression alone due to the large size of the tumor. The surgeon must always be prepared during the course of the operation for resection of the vena cava or aorta, and it is preferable that a surgeon dealing with this type of tumor be experienced in vascular surgery.

We are still in the process of evaluating the possible benefit of the preoperative aortogram. So far, it has proved to be of only limited value to the surgeon. It is a distinct aid to establishing an accurate preoperative diagnosis, but it has been our experience that even with the aid of an aortogram, the diagnostic accuracy is far from perfect. Regardless of the preoperative diagnosis, the surgeon operating upon a child with an abdominal mass must be prepared to deal with tumors and cysts of the liver, pancreas, ovary and adrenal, as well as kidney.

In our experience with 26 patients in whom the surgeon felt that the tumor had been completely removed, and in whom retroperitoneal lymph node dissection had been completed, there has been only one child who subsequently returned with metastasis. This was a child early in our series in whom a separate primary tumor in the posterior aspect of the opposite kidney was not recognized at the time of operation. All of the others are still living and free of any evidence of disease.

NEUROBLASTOMA

Neuroblastomas are probably the most common solid malignant tumors of infants and children. They arise from the sympathetic neuroblasts which occur in the adrenal gland, the sympathetic ganglia and the ectopic adrenal tissue. The tumor may be encapsulated, but more commonly it infiltrates the surrounding tissues. Widespread metastasis may occur before the primary tumor has grown large enough to be detected clinically.

When a neuroblastoma is suspected, clinical investigation in preparation for operation should be completed within a 24 hour period. An intravenous pyelogram will aid in localization of the tumor and influence the treatment. A tumor arising from the adrenal gland will displace the kidney downwards; a tumor arising from the retroperitoneal sympathetic ganglia may displace it upwards and laterally. Roentgenography of the skull and long bones, and a needle aspiration biopsy of the bone marrow are also valuable in preoperative evaluation, since bone metastasis from neuroblastoma may occur early and, when present, is a particularly ominous finding. Preoperative urinary catecholamine determination is of value in that it provides a base line level by which one can evaluate the effectiveness of subsequent therapy. Anemia, if present preoperatively, is corrected by the administration of whole blood prior to operation.

The preferred treatment of neuroblastoma consists of surgical removal of the tumor followed by roentgen therapy to the operative site. If this can be accomplished, it will result in an 85 to 90 per cent perma-



FIG. 3. A recurrent reticulum cell sarcoma removed from a 4 year old boy. Note the attached kidney and segment of intestine removed with the tumor because of apparent direct invasion. The boy is living and well 10 years later.

nent cure rate.[1] If complete removal is not possible, considerable benefit may result from removal of the greater bulk of the tumor, even though a small amount of obvious tumor is left behind. If metastasis to bone marrow has not occurred, and if postoperative roentgen therapy is carefully administered, over half of these patients will survive for 5 or more years. If the amount of the tumor can be removed safely, biopsy only, followed by roentgen therapy in the absence of distant metastases will result in approximately 35 per cent "cure" rate. A surprisingly high "cure" rate of 67 per cent results in the group with hepatic metastasis only, when roentgen therapy is administered to the liver area. Spontaneous recovery may be expected in approximately 10 per cent of all cases of neuroblastoma. There can be little doubt that permanent cure of some neuroblastomas can be attributed to roentgen therapy alone, but a higher cure rate results if it is combined with surgery.

The prognosis is considerably better in infants than it is in older children. In a certain percentage of children with neuroblastoma, hypertension and diarrhea are a prominent feature of the illness, and are associated with markedly elevated urinary catecholamines. Neither of these factors seems to bear any influence on the prognosis.

Chemotherapeutic agents in our series have been utilized only for infants with demonstrable metastasis. Roentgenographic evidence of bone metastasis has been associated with a grave prognosis regardless of the type of therapy employed. On the other hand, we have been able to salvage 5 infants with microscopic evidence of tumor cells in the bone marrow with the aid of systemic chemotherapeutic agents. These children are living and free of evidence of disease as long as 7 years later.

MALIGNANT LYMPHOMA

In our experience, surgery for malignant lymphoma has been limited primarily to a means for obtaining tissue to establish a histologic diagnosis, with a single exception. We have one boy who is living and free of any evidence of disease 10 years following radical surgery for a reticulum cell sarcoma of the terminal ileum. The operation consisted of removal of the terminal small bowel, the right colon, and the right kidney and ureter, as well as a segment of the an-



FIG. 4. Rhabdomyosarcoma of the orbit treated by radical exenteration and primary closure. Metastatic tumor was removed 6 weeks later from the pre-auricular and submandibular areas. Local cobalt 60 teletherapy was administered. There is no evidence of recurrence 18 months later.

terior abdominal wall (Fig. 3). He received a course of postoperative irradiation to the abdomen. The results in his case were gratifying, but constitute a definite exception to the rule.

RHABDOMYOSARCOMA

Our experience with rhabdomyosarcoma has been limited and rather discouraging. We have 2 relatively longterm survivals following radical surgery combined with radiation therapy. One tumor arose in the nasopharynx the other in the orbit (Fig. 4). A third child, 14 years ago, with rhabdomyosarcoma of the vagina, was treated with radiation therapy alone and is now well and free of disease. The others have all succumbed in spite of aggressive management with surgery, radiation and chemotherapy.

SUMMARY

An aggressive, optimistic attitude with a team-type approach, including the pediatrician, the surgeon, the radiologist, the chemotherapist and the pathologist, constitutes the essentials for the management of the soft tissue solid tumors of childhood.

The results can be most gratifying when dealing with infants, since instead of thinking in terms of a 5 year cure, we can proudly think in terms of our successful cases being 65 year cures.

Department of Pediatric Surgery
The Children's Hospital
240 Bethesda Avenue
Cincinnati, Ohio 45229

REFERENCES

1. Gross, R. E., Farber, S., and Martin, L. W. Neuroblastoma sympatheticum: study and report of 217 cases. *Pediatrics*, 1959, *23*, 1179–1191.
2. Martin, L. W., and Kloecker, R. J. Bilateral nephroblastoma (Wilms' tumor). *Pediatrics*, 1961, *28*, 101–106.
3. Martin, L. W. Surgical treatment of tumors. In: Pediatric Therapy. Second edition. Edited by H. C. Shirkey. C. V. Mosby Company, St. Louis, 1967, pp. 915–930.

RADIUM DOSAGE PATTERNS IN THE TREATMENT OF UTERINE CARCINOMA*

By JACOB SPIRA, PH.D., *and* ISAMETTIN ARAL, M.D.
BOSTON, MASSACHUSETTS

THE determination of the dose following Heyman's radium packing technique in the treatment of endometrial carcinoma is probably one of the most difficult tasks to perform in radiation dosimetry. A direct measurement of radiation doses is almost impossible and the only practical way of indirect dosimetry remains the introduction of a small probe into the rectum and the bladder. These measurements, while providing a certain guideline for the physician as far as biologically safe doses to the rectum and the bladder are concerned, do not permit any valid estimation of the dose distribution around the uterus. This cannot be accomplished either by measurements or calculations of the dose to Point A (from the Manchester system) or to Point C on the outer surface of the uterus as suggested by various authors. It would seem that the best results could be achieved by actual measurements of the radiation doses around the periphery of the uterine phantoms. Indeed, few authors have investigated the dose relationship between the size of the uterus packed with radium and the dose rate to the few points distributed on the periphery of the uterine phantom; their results have indicated definite limitations in the uniformity of irradiation imposed upon the method by irregularities in the shape of the uterus.

The authors have initiated the investigation of the dosimetry of the radium treatment of endometrial carcinoma because of the following reasons: first, we did not believe that the uniformity of the dose distribution at the points equidistant from the uterine wall could be postulated; one look at the shape of the uterus packed with radium will show that quite large discrepancies have to be expected. Furthermore, we could not agree with statements of some investigators who have measured the "average" dose at 0.5 cm. from the uterine wall for a few sets of radium capsules-uterus size combinations and extrapolated this number to larger or smaller uteri. As a matter of fact, we felt that an average dose along the uterine wall might have a meaning only if as many points along the periphery as possible are measured. Even then, the value of the average dose might be questionable as far as dose-effect relationship is concerned, and should be replaced by maximum and minimum dose limits along the uterine wall. Finally, we intended to divide the uterine cavity into 3 parts and to evaluate experimentally the average dose to each part separately. From all of these measurements we hoped to find some relationship between the size of the uterus as shown by the number of packed radium capsules and the distribution of radiation dose around the wall of the uterine cavity. If these evaluations were correct, a way could be found to extrapolate the average or maximum and minimum doses to any uterus-radium number combinations and thus permit the physician a more accurate evaluation of the doses delivered in each individual patient's case. In addition, it is believed that the determination of the doses in roentgens or rads to very definite points and areas around the uterine cavity is of a definite advantage in the evaluation of the dose-effect relationship in the treatment of the endometrial carcinoma.

The experimental set-up used for the determination of the dose in simulating Heyman's technique was the following: 4

* Presented at the Sixty-eighth Annual Meeting of the American Roentgen Ray Society, Washington, D.C., September 26–29, 1967.
From the Department of Radiation Physics and the Department of Radiotherapy, Boston University Medical Center, Boston, Massachusetts.

different cavities simulating different sizes of uterus were carved in large blocks of paraffin which were afterwards cut in the middle along the sagittal plane. Along the periphery of each uterine phantom, holes were drilled at the distance of 0.5 cm. from the wall, the distance being measured radially from the imaginary center of the uterine cavity. In addition, holes were drilled in positions corresponding to Points A and B as well as V and R from the cervical carcinoma terminology, the latter representing the posterior part of the bladder and the anterior part of the rectum. As radiation detectors, Sievert miniature ionization chambers and lithium fluoride powder capsules were used alternatively (Fig. 1). Detectors were inserted into the proper openings, the two parts of the phantom pressed together and kept tight during the entire procedure. Radium capsules were inserted through the simulated vagina and after completion of the uterine packing, a capsule was left in the cervix uteri. Upon termination of the procedure, a roentgenogram was taken and the position of each capsule was studied.

For each phantom and its associated radium content, several consecutive measurements were performed, re-inserting the

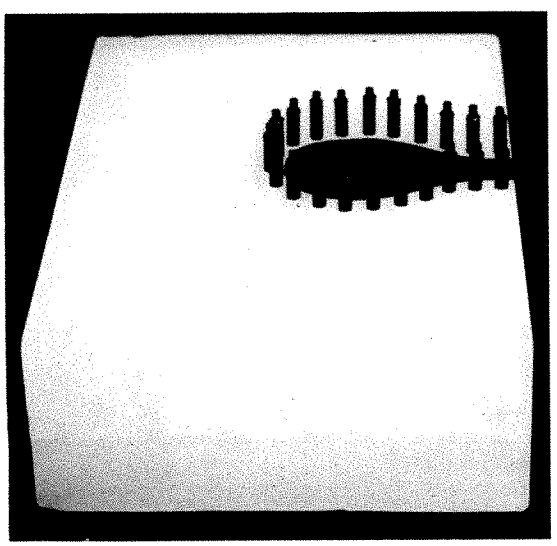


Fig. 1. Paraffin model of the uterus with lithium fluoride capsules inserted around the periphery.

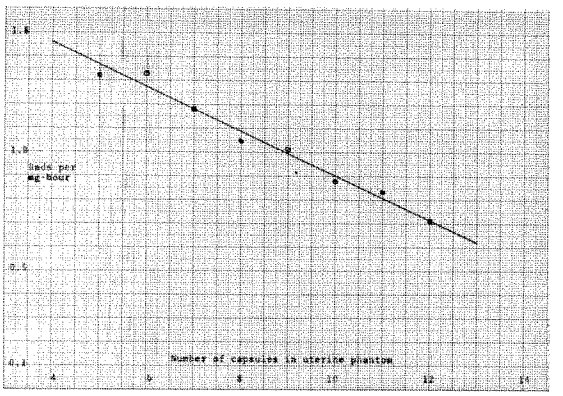


Fig. 2. Experimentally measured average doses in rads per mg.-hr. for different number of capsules in uterine phantom.

radium capsules the same way as explained above and re-charging the detection chambers. While analyzing hundreds of data accumulated in multiple repeated experiments, we were unable to come up with a reproducible pattern of dosimetry. We have attempted to study the reasons for this failure, and it seems to us that there is a sharp dose gradient along the periphery of the uterus at such short distances from the radium capsules that we have measured. These gradients cannot be measured with detectors of appreciable size as compared to the distances at which the measurements were performed. Following this assumption, we repeated all the previous measurements using Adlux film cut exactly to the size and form of the uterus and sandwiched between the two planes of the paraffin phantom. Results of the photographic measurements are presented in the enclosed graph (Fig. 2). It is important to note that each point on the graph represents results of 5–10 separate experiments and in each experiment the dose represents the average of 18 points measured on the exposed film. Although the mathematical limits of the average dose will be discussed later, it suffices to say that the results do point out to a definite pattern indicating that the average dose in rads/mg.-hr. of radium at 0.5 cm. from the uterine wall can be calculated and extrapolated for any reasonable

number of radium capsules. During our measurements and calculations, however, it became evident that the concept of the average dose around the wall of the uterine cavity will hardly contribute to the evaluation of the biologic effects of radiation in the uterus. The doses in different points around the same uterine cavity differed widely and the arithmetic average seemed only to indicate roughly the relation between the average dose in rads and a given number of implanted uterine applicators. However, much more information can be obtained by dividing the uterine investigated cavities into 3 arbitrary zones and by calculating the average doses for each particular zone and then comparing the same zones of different uteri. The indication of the minimum and maximum dose around the particular cavity as well as the doses to Points A, B, V and R together with the average dose should constitute much firmer basis for biologic evaluation.

It was apparent from the beginning of our experimental work that the main difficulty lies in the nonreproducibility of the radium capsules pattern within a uterine phantom. Even with the greatest care and effort one could not reproduce the same geometric placement of radium capsules using the same phantom and the same number of capsules. Every consecutive radium packing performed as described previously, differed in geometry from the previous one and consequently two identical uterine radium implants showed significantly different dose distributions. A slight change in a position of one or more capsules within the cavity seemed to cause a significant difference in local and average dosage. Indeed it became important to verify our numerous but quite scattered data with some system, where the geometric distribution of capsules could be reproduced or easily determined, and the doses from each capsule to different points of interests quickly calculated. If this system proved operable, the way would be open to the ultimate and complete solution of the dosimetry in the treatment of endometrial carcinoma by Heyman's method.

A computer program was written to calculate the dose distribution from radium capsules packed in uterine cavity. An IBM computer system was used to perform the necessary calculations. A uterine phantom is filled with Heyman capsules, emptied of radium content. The location and orientation of each capsule is defined geometrically by measuring and recording on punched cards the cartesian co-ordinates of a point at each end of the capsule. As there are 3 co-ordinates for each point and 2 points for each capsule, 6 data values must be given for each capsule.

The first action of the program is to read into memory a group of cards, one card for each capsule, which describes the constellation in numerical terms. To check the accuracy of these data, the geometric length of each capsule is printed and compared to the actual length of 1.87 cm. Since the length of the radium salt is shorter than the metal case around it, the co-ordinates of the end of the capsule are adjusted internally, to make the active length of each capsule 1.5 cm. In order to compute the total radiation dosage to any point around the radium capsules constellation, the 3 co-ordinates defining the point of interest are punched on the card and read by the program into the computer. The dosage contributed to the point by each capsule is calculated by evaluating Sieverts' integral, substituting appropriate angles and radium into the original equation. These partial dosages are then summed to give the final answer which is printed along with the intermediate results.

The program then reads the co-ordinates of the next point and computes the dosage it receives, until the total number of points has been exhausted. A summary of the results is printed and the entire cycle is repeated from the beginning by defining a different constellation and a new set of dosage points.

Results of the computer calculations are

presented in the enclosed graph (Fig. 3). Each point represents two consecutive calculations with slightly changed distribution of radiation capsules. For comparison reasons, the results of previously discussed experimental measurements are also included. It is interesting to note, that the 2 curves differing slightly quantitatively, have similar slopes indicating that there is a definite pattern in average doses as a function of number of radium capsules. In order to increase our information concerning the dose distribution we have extracted from the computer the maximum and minimum dosage data associated with each implant and plotted them together with the average dose curve (Fig. 4). Few interesting conclusions can be derived from this plot: it appears that the maximum and the minimum dosage for different radium capsules number follows more or less similar pattern. One can easily calculate the percentage difference between the average dose around the wall of the uterus and the maximum or minimum dose for each radium-uterine size pattern. In our example, 5 capsules implant shows the difference of ±15 per cent, 8 capsules of ±32 per cent, 10 capsules of ±35 per cent and 12 capsules of ±42 per cent.

It is conceivable that this information coupled with the average dose delivered to the wall of a particular uterus, stating the actual limits of the dosage in rads, could be of aid in evaluation of the biologic effects of radiation delivered. Still, one can find more detailed information in the next graph (Fig. 5), where the average doses in the 3 zones of the uterus are plotted for each radium-uterus combination, as well as the doses to Point A and B. Zone I = cervix uteri; Zone II = corpus uteri; and Zone III = fundus. These zones are arbitrarily marked on all 4 uterine phantoms and the average doses for each zone plotted against the number of radium capsules. The graph supplies information as to the average dose distribution around each zone of uterus, for

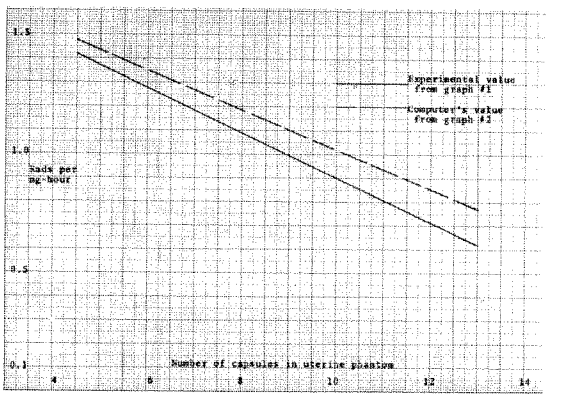


Fig. 4. Comparison of computer calculated and experimental doses in rads per mg.-hr. for different number of capsules in uterine phantom.

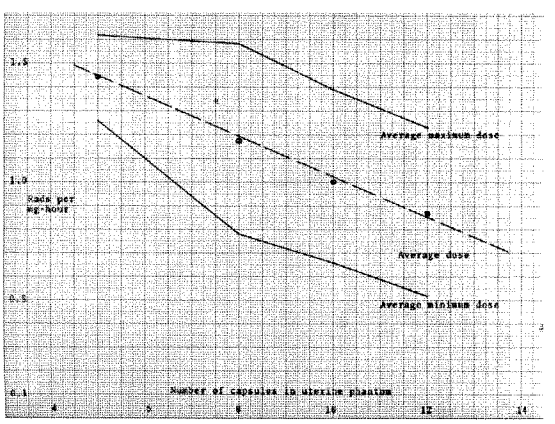


Fig. 3. Computer calculated average maximum and minimum doses in rads per mg.-hr. for different number of capsules in uterine phantom.

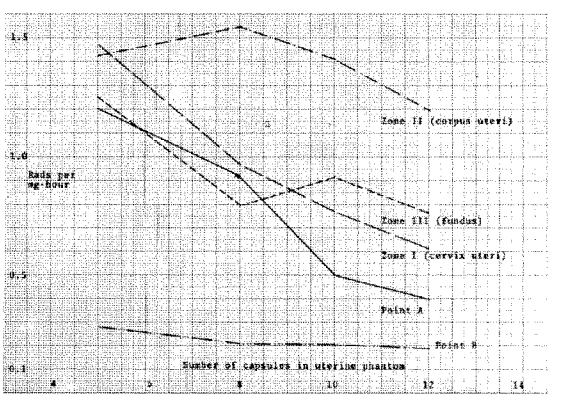


Fig. 5. Computer calculated average doses in three different sections of the uterus in rads per mg.-hr. for different number of capsules in uterine phantom.

all the uterine phantoms we have measured. It is interesting to note that with the uterine sizes packed with 5–12 radium capsules, Zone II (corpus uteri) which due to its central position bears the heaviest impact of radiation, shows the smallest percentage changes in radiation dosage. If we were to calculate the average value for Zone II, all Zone II values would fall within ±15 per cent of the average. For Zone III (fundus) the deviation from the average is ±25 per cent, and for Zone I (cervix uteri) ±40 per cent. While it is true that the majority of the uterine lesions are located in the corpus uteri or the fundus, and most probably in the corpus uteri, the considerable drop of the dose in the cervix uteri should be of importance in view of the established practice of leaving one capsule in the cervix to prevent the spread of the disease to the upper third of the vagina. The graph also shows the doses calculated to Points A and B. While certain information related to the dosimetry of the system could be eventually derived from the dose to Point A, none whatsoever can be obtained from the knowledge of the dose to Point B. On the whole, it is believed, that both graphs with their detailed information about the average dose around the uterus, the maximum and the minimum dose, the average doses in each separate zone of the uterus, and finally the dose to Point A, for all investigated uterine phantoms packed with the corresponding amount of radium capsules will permit the physician much more accurate evaluation of the dose-effect relationship in the treatment of the endometrial carcinoma.

SUMMARY

In the radium treatment of endometrial carcinoma using Heyman's packing technique, variations in shape and size of malignant uteri become very important in evaluation of the dose delivered to uterine walls and the adjacent structures. Because of these difficulties, an unsatisfactory method of stating dosage in milligram-hours of radium has been retained in gynelogic curie therapy.

An experimental program to determine the distribution of radiation along the periphery of the uterine wall as well as to structures of anatomic importance was recently completed. Multiple measurements were performed in different sizes of uterine models using Sievert miniature ionization chambers, lithium fluoride dosimeters and slow films. A limited computer program was written to check the pattern of experimental measurements. The results were satisfactory and an extensive computer program was started to develop a system of complete radium dosage patterns for uterine cavities of different size and shape and their associated radium content.

Jacob Spira, Ph.D.
Department of Radiation Physics
Boston University Medical Center
Boston, Massachusetts 02118

REFERENCES

1. EVANS, W. E., and MABBS, D. V. Dosage control of direct measurement in radium treatment of uterine carcinoma. *J. Fac. Radiologists*, 1958, *9*, 66–67.
2. HUNT, H. B. Comparative radiotherapeutic results in carcinoma of endometrium as modified by prior surgery and post-irradiation hysterosalpingo-oophorectomy. *Radiology*, 1956, *66*, 653–666.
3. LOEFLER, R. K. System of radium distribution for treatment of cancer of corpus uteri. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1955, *73*, 425–436.
4. NOLAN, J. F., and STEELE, J. P. Carcinoma of endometrium: measurements of radiation distribution around various multiple capsule applications of radium in irregular uteri. *Radiology*, 1948, *51*, 166–176.

VOL. 105, NO. 1

A SIMPLE MODIFICATION OF THE STOCKHOLM APPLICATOR FOR THE TREATMENT OF EARLY CANCER OF THE UTERINE CERVIX*

By GHOLAM H. ZARGHAMI, M.B., CH.B.,† *and* SAMUEL S. KUROHARA, M.D., PH.D.‡
With the Technical Assistance of Lavern Clay
BUFFALO, NEW YORK

THE Stockholm technique of radium treatment which was initiated by Forsell in 1910, and developed by Heyman, is based on the following principles:

1. The function of radiation therapy with an intra-uterine radium applicator is to deliver irrecoverable damage to the local tumor, and at the same time, keep the dose to neighboring, apparently normal, structures low enough so that these can recover.
2. While it is possible in such lesions that microscopic spread of the disease to other pelvic structures has occurred, it is almost futile to attempt control of such potential extensions with an intra-cavitary applicator alone. For this reason, treatment is planned only to include the local tumor and a minimum of its surroundings.
3. The treatment is fractionated into two or more exposures, delivering relatively high intensity radiation over relatively short periods.
4. A variety of applicators of different sizes permits the use of an applicator which particularly suits the individual patient's anatomy.

Although the Swedish method has yielded excellent results in highly experienced hands, a disadvantage, which perhaps has limited its widespread use at least in the United States, is the difficulty of maintaining the proper relationship between the uterine tandem and the vaginal plaque.

While the tandem should be perpendicularly applied to the center of the plaque, the ideal position is almost never attained and is not practicable, especially in advanced lesions that are grossly asymmetric. In most Stage I lesions it is preferable that the tandem be centrally placed on the plaque, although it need not be perpendicular to it.

The purpose of this paper is to present a single simple modification, which we hope will improve the attainment of good positioning and will generally simplify the procedure.

MODIFICATION OF THE STOCKHOLM APPLICATOR

At the Roswell Park Memorial Institute, the Stockholm tandem and plaque are used for most of the early cases of cervix cancer. The apparatus and radium loading have been described by others.[1,2] Our simple modification consists of the attachment of a 1 cm. long stem to the lower end of the tandem (the screw-cap end) and the placement of a circular opening with beveled

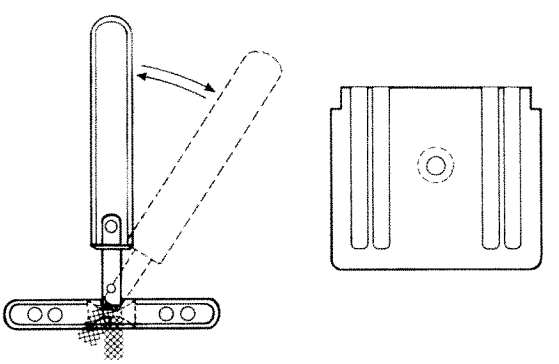


FIG. 1. Diagram of the modified Stockholm applicator for treatment of early cancer of the cervix.

* From the Departments of Gynecology,† and Radiation Therapy,‡ Roswell Park Memorial Institute (New York State Department of Health), Buffalo, New York.

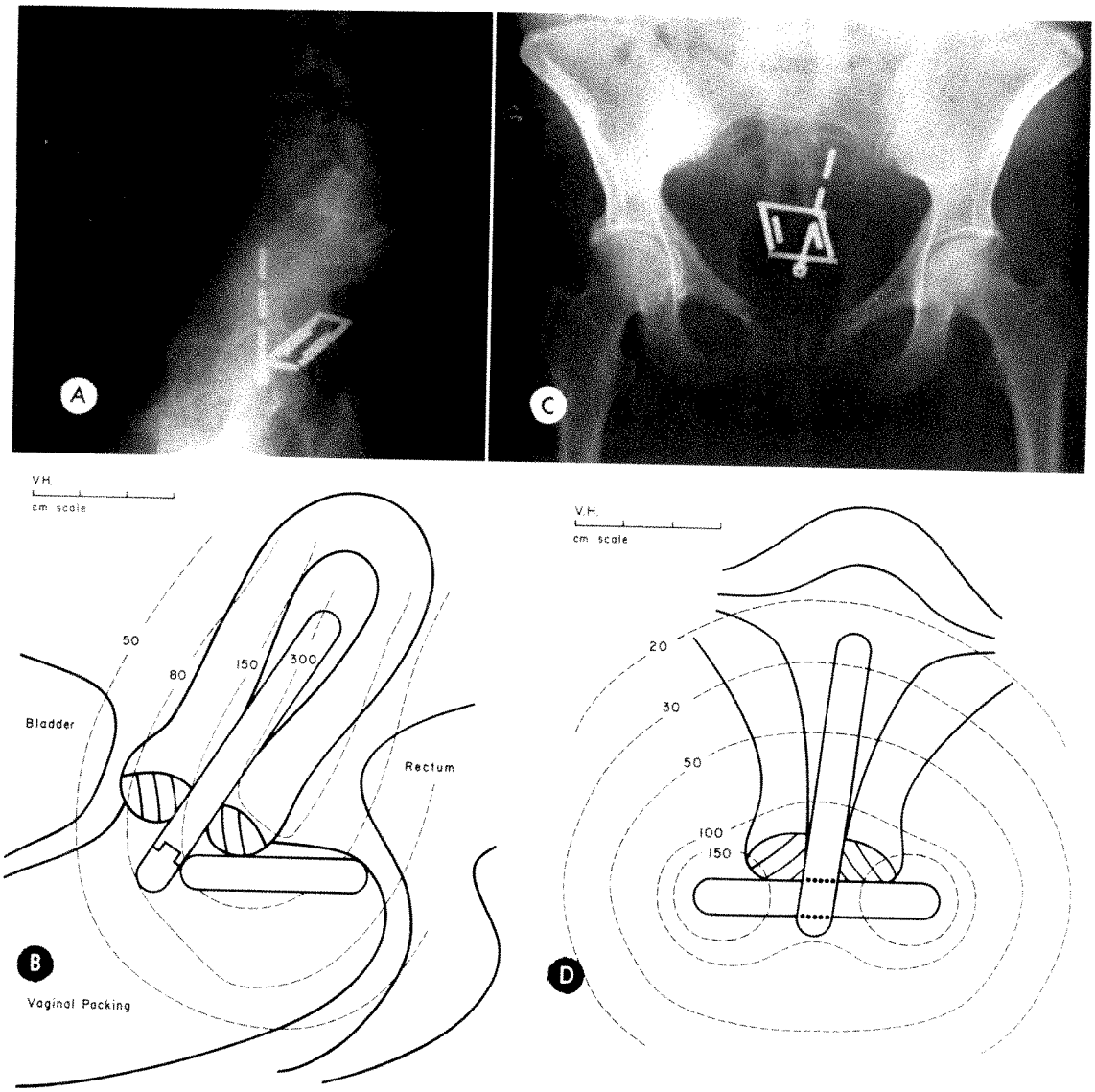


FIG. 2. Case 1. (*A*) Lateral localization view. (*B*) Anteroposterior isodose distribution plane through the cervical os, perpendicular to plaque. Note the high dose received by the anterior rectal wall as compared to the anterior extent of cervical tumor. (*C*) Anterior localization view. (*D*) Lateral isodose distribution through cervical os perpendicular to plaque. Note that the curves are flattened, superiorly and inferiorly. Dosage distribution was computed by a previously described procedure[5] after standardizing with an experimentally determined value at several points.

edges in the center of the plaque. The stem fits loosely within this hole.

This arrangement prevents displacement of the tandem from the center of the plaque but allows the uterine fundus to attain its natural position in relation to the vagina. The opening in the plaque is large enough for the stem of the tandem to slip in with ease, and the beveled edge to permit the tandem to tilt in all directions to describe a 45° cone. The amount of tilt gives sufficient flexibility to accommodate individual variation in the position of uterus. A 1 cm. stem has been found to be long enough to hold the lower end of the tandem in place and not interfere with application of the plaque against the cervix (Fig. 1).

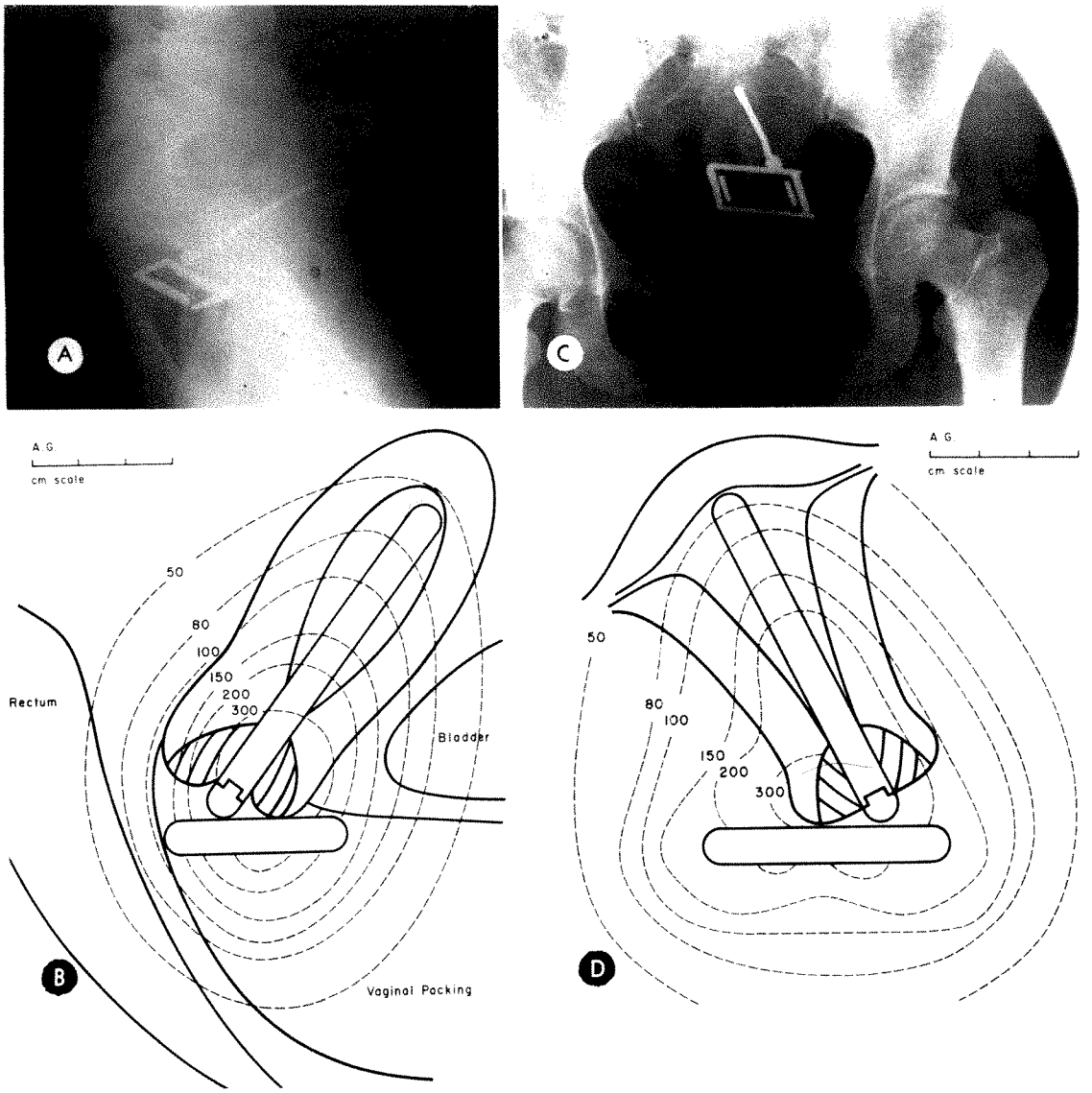


Fig. 3. Case II. First application by conventional method. (*A*) Lateral localization view. (*B*) Anteroposterior isodose distribution plane through cervical os, perpendicular to plaque. (*C*) Anterior localization view. (*D*) Lateral isodose distribution through cervical os perpendicular to plaque. Note the high dose received by the right paracervical region as compared to the left.

This method has been in use at this Institute for the last 6 months and there has not been an instance when the stem has slipped out of the opening in the plaque following adequate packing.

The following two cases will illustrate the advantages of this modification.

REPORT OF CASES

Case I. This patient had a Stage I, large, (tumor size—approximately 4×5 cm.) squamous cell carcinoma of the uterine cervix. A 7 cm. long tandem, containing three 25 mg. radium tubes, and a 4×5 cm. plaque, containing a 10 mg. and two 15 mg. tubes at each lateral shorter end, were applied. Figure 2, *A* and *B* shows that the tandem is displaced totally anteriorly completely off the plaque. Figure 2, *C* and *D* reveals that the rectum receives more radiation than the anterior margin of the tumor. This radium application was discontinued after 4 hours. The patient had to undergo the risk of another anesthesia and the

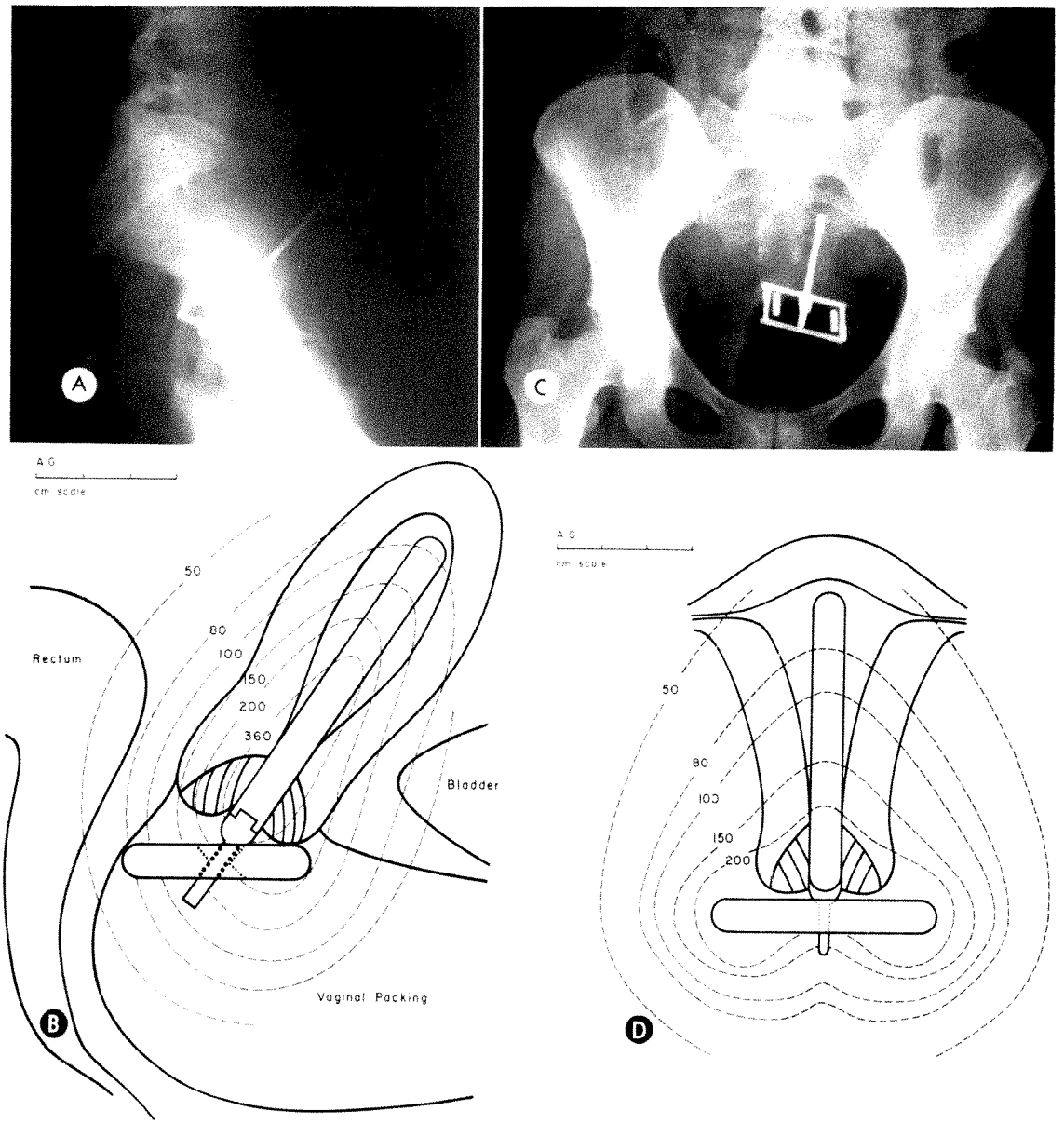


FIG. 4. Case II. Second application by modified method. (*A*) Lateral localization view. (*B*) Anteroposterior isodose distribution plane through cervical os, perpendicular to plaque. (*C*) Anterior localization view. (*D*) Lateral isodose distribution through cervical os perpendicular to plaque. Note that both paracervical areas receive similar doses.

Institute had to sustain the extra cost of hospitalization at the time of reinsertion.

CASE II. This patient was found to have a Stage I, large, (tumor size—approximately 3×3 cm.) squamous cell cancer of the cervix. An 8 cm. long tandem, containing two 25 mg. and two 20 mg. radium tubes, and a 4×5 cm. plaque with the same loading as the previous case, were applied for 26 hours. Figure 3, *A* and *B* shows that the lower end of the stem is displaced posterolaterally to the left of the center of the plaque. Figure 3, *C* and *D* reveals the underdosage of the posterior and left lateral aspect of the tumor and the overdosage of the uninvolved normal tissue anterior and right lateral to the cervix and fornix. The modified technique was employed 3 weeks later. Figure 4, *A* and *B* shows the very satisfactory position of the tandem relative to the plaque, and

Figure 4, *C* and *D* demonstrates the optimal radiation dose distribution.

DISCUSSION

In 1938, Tod and Meredith[6,7] introduced the concept of "Point A" and "Point B" in the radium treatment of cancer of the uterine cervix. Point A was taken to be 2 cm. lateral to the central canal of the uterus and 2 cm. from the mucous membrane of the lateral fornix in the axis of the uterus, Point B being 5 cm. from the mid-line and on the same level as Point A. Point A is in the paracervical triangle, which is in reality a pyramid with its base resting on the lateral fornix and the apex curving round with the anteverted uterus. Point A is where the uterine artery crosses the ureter. According to Tod and Meredith, the initial radiation necrosis is always due to the high dose effect in this paracervical region and not a direct effect on the rectum.

According to Kottmeier,[3,4] the dose at Point A with the Stockholm tandem and plaque in gamma roentgens is numerically about equivalent to the milligram-hours. However, it should be realized that this is true only in a hypothetical situation where the tandem is perpendicular to the plaque and where there is no displacement of the plaque. In practice, this is almost never the case. If roentgenograms are not routinely taken after each application of radium, this can be overlooked.

Table 1 shows the variation in Point A doses that can occur in a few hypothetical situations where the tandem is tilted laterally and/or displaced laterally from the center of the plaque. It also shows the variations encountered in the 2 cases presented.

TABLE I

VARIATION IN POINT A DOSE DUE TO DISPLACEMENT AND/OR TILT OF TANDEM RELATIVE TO PLAQUE

A. Model Tilt	Displacement*	Ratio of Point A Doses High A/Low A
20° Right	none	1.43
20° Right	1/4	1.03
20° Left	1/4	1.65
40° Right	none	2.10
40° Right	1/4	1.15
40° Left	1/4	3.87
B. Cases		
I.		1.08
II. First application		1.96
Second application		1.00

* 1/4 width of plaque to the right.

CONCLUSION

This modification seems most suitable for early lesions. At this Institute, this modification is being used regularly and although the number of patients treated is not large enough to warrant a statistical assessment, all the applications have been satisfactory. Final judgment depends on the follow-up of patients treated in this manner, and a comparison of the results with those of the conventional Stockholm applicator.

Samuel S. Kurohara, M.D.
Department of Radiation Therapy
Roswell Park Memorial Institute
666 Elm Avenue
Buffalo, New York 14203

REFERENCES

1. Graham, J. B., Sotto, L. S., and Paloucek, F. P. Carcinoma of the Cervix. W. B. Saunders Company, Philadelphia, 1962.
2. Kjellgren, O., and Ragnhult, I. Armamentarium for radium treatment of carcinoma of uterine cervix. *Acta radiol.* (Therapy), 1963, *1*, 1–22.
3. Kottmeier, H. L. Carcinoma of the Female Genitalia. Williams & Wilkins Company, Baltimore, 1953.
4. Kottmeier, H. L. Surgical and radiation treatment of carcinoma of uterine cervix: experience by current individualized Stockholm technique. *Acta obst. et gynaec. scandinav.*, 1964, *43*, 1–48.
5. Powers, W. E., Bogardus, C. R., Jr., White, W., and Gallagher, T. Computer estimation of dosage of interstitial and intracavitary implants. *Radiology*, 1965, *85*, 135–142.
6. Tod, M. C., and Meredith, W. J. Dosage system for use in treatment of cancer of uterine cervix. *Brit. J. Radiol.*, 1938, *11*, 809–823.
7. Tod, M. C. Optimum dosage in treatment of carcinoma of uterine cervix by radiation. *Brit. J. Radiol.*, 1941, *14*, 23–29.

A NEW RECTAL DOSIMETRY CATHETER FOR USE IN RADIATION THERAPY OF CARCINOMA OF THE UTERINE CERVIX*

By J. J. SHELDON, M.D., M. VUKSANOVIC, M.D., G. J. WOLD, M.S., *and* E. A. FONTS, M.D.
MIAMI, FLORIDA

RADIATION damage to the rectal mucosa has long been recognized as a complication in intracavitary radium treatment of carcinoma of the cervix.[4,9,11] Through increased clinical acumen, the incidence of irreversible rectal reactions has been decreased without factual knowledge of the rectal dose. With the development of ionization chambers[2,5,12] and other radiation measuring devices[1,3,9,13,14] small enough to be placed within the rectum, the actual dose to this area expressed in gamma r can be measured The diversity of dosimeters in clinical use today reflects the desire of the therapist to determine more accurately the tolerance of the rectal mucosa.

In an attempt to obtain as accurate rectal measurements as possible, we have designed a dosimeter using a known radiation measuring device. This consists of lithium fluoride[3] capsules inserted in a flexible catheter. This catheter, which we call a "rectal dosimetry catheter," is flexible and follows the contours of the rectum. It can be left in place for long periods of time while the patient is supine in bed under actual conditions of treatment. Thus, the dose is determined without distortion of the pelvic anatomy as occurs in the dorsal lithotomy position or with the rigid probe type instruments.[6,10]

The purpose of this paper is to compare the measurements of our indwelling flexible rectal dosimetry catheter with the rigid scintillation probe[6,10] that is in general clinical use.

DOSIMETRY

Radiation dosimetry utilizing the thermoluminescence of lithium fluoride has been described in detail in the literature.[3,8] The dosimeters used consisted of polyethylene capsules containing approximately 60 mg. of powdered lithium fluoride phosphor (Fig. 1*A*). Prior to placement within the dosimeters, the phosphor is processed by standard annealing procedures.[3]

The doses received by the dosimeters are determined with a read-out device built at this laboratory (Fig. 2). This device records the emitted light from the heated lithium fluoride via a photo-multiplier tube, and the resultant current is fed to an electrometer circuit with a digital output.

The LiF dosimeters are calibrated by exposure to Co^{60} gamma rays. During exposure, they are enclosed in an equilibrium shell of 3 mm. lucite. The exposure rate at the point of irradiation is measured with a Victoreen-r meter calibrated by the National Bureau of Standards. In agreement with other investigators,[3,11,16] the response curve is essentially linear in the 20 to 800 r range that was needed for the study. Multiple readings with the system are reproducible to a standard deviation of 2.3 per cent.

Rectal dosimetry catheters are prepared by placing 8 LiF dosimeters in tandem within a 3/16 inch lumen plastic tube (Fig. 1*B*). Lead shot are inserted between every second dosimeter and at each end to permit roentgenographic visualization when the catheter is implanted. A small piece of gauze is packed into the tip end to prevent leakage of fluid into the catheter. This end is then sutured and trimmed to present a smooth, blunt surface for insertion. When assembled, the catheter is thought to be sufficiently flexible to adjust to the normal

* Presented at the Fiftieth Annual Meeting of the American Radium Society, Miami Beach, Florida, April 7–11, 1968.
From the Department of Radiology, University of Miami School of Medicine, Miami, Florida.

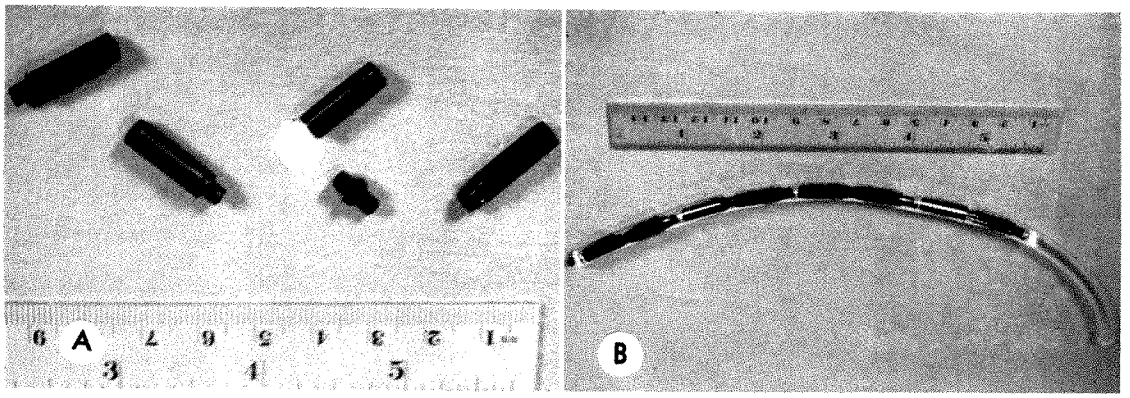


FIG. 1. (*A*) Lithium fluoride phosphor within the polyethylene capsules. (*B*) The capsules are then inserted in a plastic catheter.

anatomic contour of the rectum and the rectosigmoid.

Rectal measurements were also made with a scintillation probe. The probe is calibrated by insertion into a lucite block so that the sensitive volume of the probe is at a distance of 2 cm. from a radium source. The probe is then adjusted to read a calculated exposure in this position. LiF and probe measurements made at the same point of irradiation were consistent within ± 3 per cent.

PROCEDURE

After placing a radioactive system in the vagina and the uterus, the dose rates in the rectum were obtained by inserting the rigid scintillation probe (Probitron) and obtaining measurements at 1 cm. intervals. If the exposure expressed in r/hr. in the rectum was found to be excessively high, not infrequently the patient had to be repacked until a more acceptable arrangement was achieved. Immediately following the measurements with the rigid system, the rectal dosimetry catheter was placed in the rectum, with the distal tip taped to the skin to contain the system in place. On the localization roentgenograms of the pelvis, the anatomic relationship of the indwelling rectal dosimeter could readily be established (Fig. 3, *A* and *B*; 4, *A* and *B*; and 5, *A* and *B*). In a few initial cases, the rectal dosimeter was removed some 8 hours following anesthesia. Later, when it was apparent that the catheter in the rectum was not an added discomfort to the patient, the indwelling rectal dosimeter was kept in place up to 17 hours and the integrated dose rate was usually reported within 24 hours after the radium application.

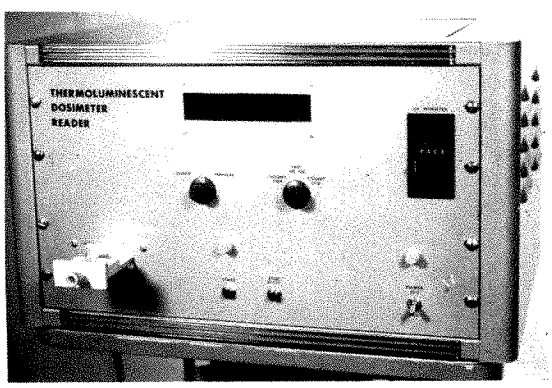


FIG. 2. Lithium fluoride read-out device with feeding pan in lower left hand corner and digital output noted in upper right hand corner.

Inasmuch as the sensitive centers of the capsules were 2 cm. apart, the dose was reported per each 2 cm. interval of rectum distally from the anus. Convenient comparison with the dose rate recorded at 1 cm. intervals by the rigid system under operating room conditions became possible.

OBSERVATIONS

The procedure was performed in 15 patients. Some of these patients had more than 1 intracavitary application, so that a total of 21 comparative measurements were

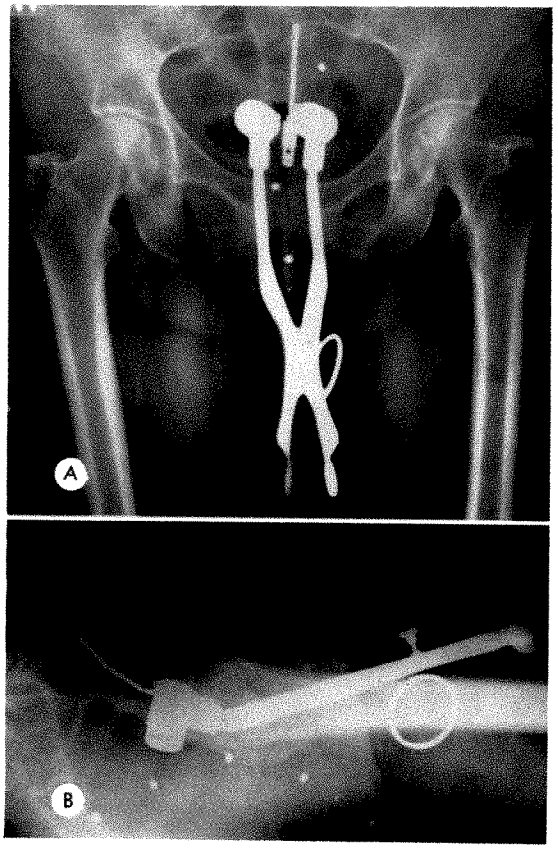


FIG. 3. (*A* and *B*) There is lead shot at the tip and between every two capsules outlining the rectal dosimetry catheter which curves posteriorly at the level of the ovoids.

studied. The average distance of insertion from the anus was 10.6 cm. with the rigid probe and 11.2 cm. with the flexible rectal dosimeter. The dose rates obtained by the rigid probe were significantly higher in 15 of the 21 applications. This higher dose rate difference became apparent at a distance of several centimeters from the anus (Fig. 3*C*). This difference averaged some 26 rads. The higher readings obtained with the rigid dosimeter were encountered between 3 to 8 cm. from the anus. In 6 radium applications, the readings obtained by both dosimetric systems were not significantly different, while in a single instance the dose rate recorded by the Probitron was lower than that obtained by the indwelling flexible dosimeter (Fig. 4*C*; and 5*C*).

DISCUSSION

During intracavitary radium applications, the vaginal vault is frequently distended by the gauze packing, resulting in flattening of the rectum in its fixed portion at the level of the rectovaginal septum.[6,7] Consequently, the readings obtained in the first 5 to 6 cm. from the anus would be similar using both the rigid and flexible dosimeters. More distally, however, the posterior inflection of the rectosigmoid would not permit reproducible measurements with the rigid dosimeter, as it was more subjected to variations of position relative to the vaginal radium. At this point the readings with the rigid system were usually greater. One could speculate that the rigid dosimeter would displace this portion of the rectosigmoid anteriorly, bringing the mucosa closer to the radium system. The flexible dosimetry catheter, curved posteriorly with the

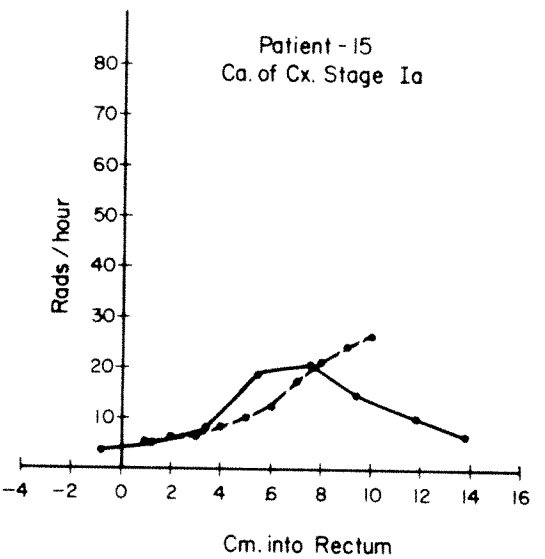


FIG. 3. (*C*) The dose rates of the probe and the dosimetry catheter are similar up to 6 cm., which is the level of the vaginal radium. The rigid probe cannot bend posteriorly, hence the dose rate it records continues to increase. The dosimetry catheter curving posteriorly measures a decreasing dose rate.

rectosigmoid, would more realistically represent the energy absorbed by the mucosa at that level.

In studying the roentgenograms of the 5 intracavitary radium applications in which the readings with the rigid probe, as well as with the indwelling rectal dosimeter, were similar, it could be noted that the inflection of the indwelling catheter was less pronounced, hence losing the advantages of the flexibility previously described (Fig. 4, *A* and *B*). In a single instance in which the readings with the rigid probe were lower than with the flexible catheter, the roentgenogram clearly indicated that the coiling of the catheter in the rectum was giving false high readings (Fig. 5, *A* and *B*).

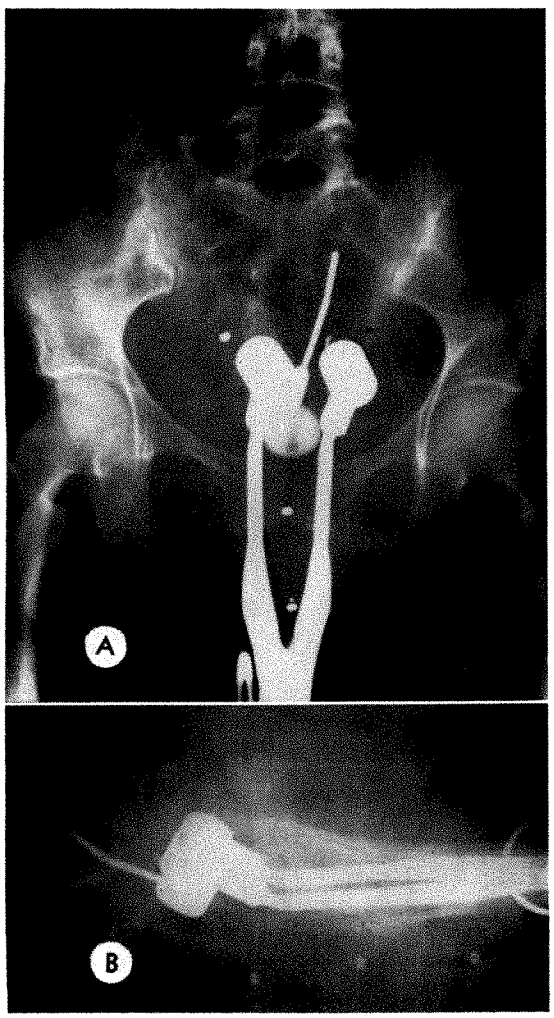


FIG. 4. (*A* and *B*) The dosimetry catheter is straight from the anus to its tip which is past the level of the ovoids.

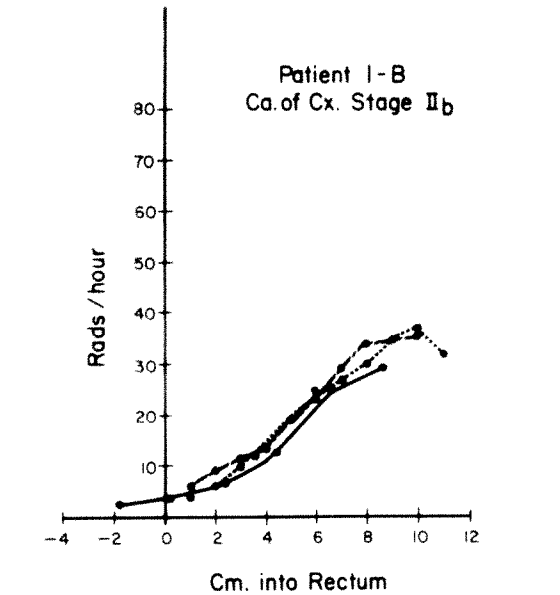


FIG. 4. (*C*) The rectal dosimetry catheter, being straight, records a dose rate that shows no significant difference from that recorded by the rigid probe.

CONCLUSIONS

From the experience gained in comparing the dose rates obtained at the level of the rectum during intracavitary radium applications for gynecologic malignancies, it appears:

(a) Both systems of dose measurements are fairly similar to a distance of 6 cm. from the anal sphincter.

(b) From the point that the rectosigmoid curves posteriorly, the rigid dosimeter conceivably gives a false higher dose rate by virtue of bringing the rectal mucosa closer to the radium system.

(c) The advantage of the flexible rectal dosimeter consists in eliminating this

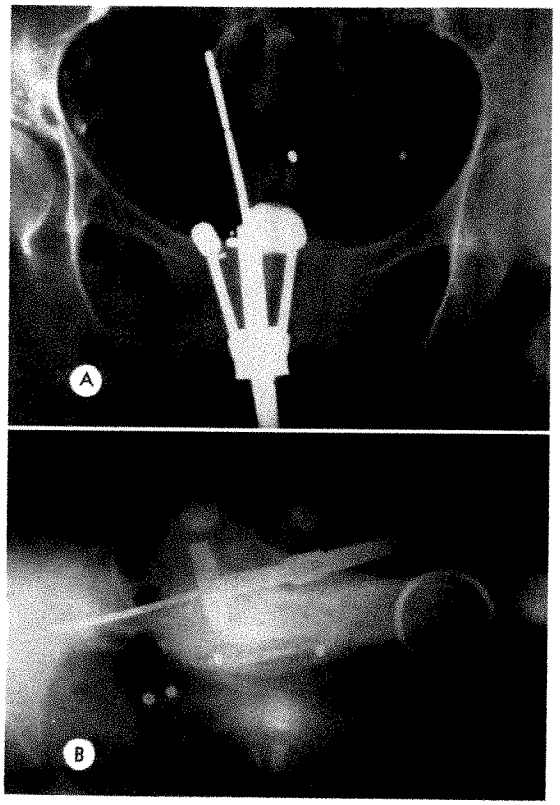


FIG. 5. (*A* and *B*) The dosimetry catheter is coiled in the rectum at the level of the vaginal ovoids, hence it does not record a dose rate 10 cm. from the anal verge, but rather a dose rate for 10 cm. of dosimetry catheter.

factor of error and following more closely the anatomy of the rectum and rectosigmoid.

(d) The fact that both dosimetric procedures have very close, or similar, efficiency up to 5 to 6 cm. from the anal sphincter, indicates the relative usefulness of the rigid system also, inasmuch as at this level the greater proportion of serious sequelae do occur (proximity to the vaginal radium).

(e) The advantage of LiF in itself, at least theoretically, is that it should reflect more closely the accumulated dose throughout several hours of exposure in a patient under actual conditions of treatment.

(f) The anatomic relationship of the rectal dosimeter can be clearly established by roentgenograms obtained of the patient following intracavitary radium procedures, thus permitting the predictability of the region of a possible high dose rate.

(g) The speculations as to the dose range of tolerance of the rectum to the gamma radiations from radium are beyond the scope of this work, and follow-up of patients, continuing comparison, and careful dose measurements may offer this opportunity in the future.

SUMMARY

Irreversible radiation damage to the rectal mucosa is an avoidable complication of

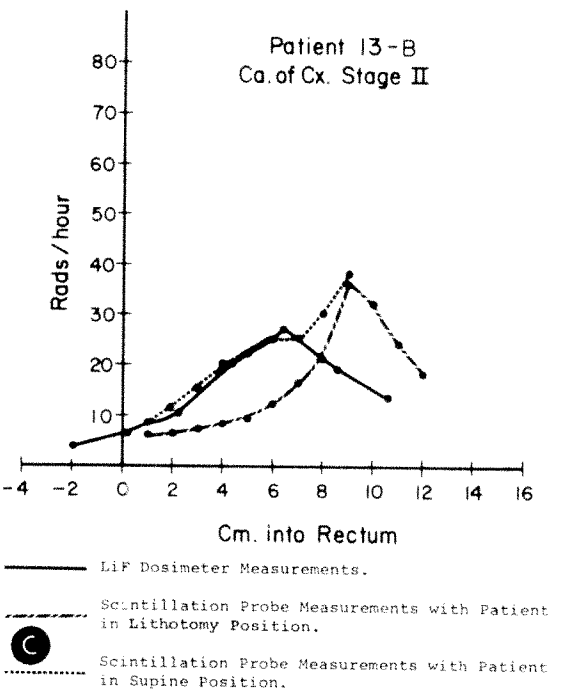


FIG. 5. (*C*) The dose rate is higher than the probe readings as the coiled dosimetry catheter has most of its radiosensitive LiF capsules at the level of the radium. The catheter tip, however is lateral to the radium, thus recording lower dose rate at the point of maximum insertion (10 cm.). This cannot be compared with probe measurement at that distance as the probe was measuring 10 cm. from anus while the dosimetry catheter, because of its coiling, was not.

intracavitary radium treatment of carcinoma of the cervix. In order to minimize this kind of complication, the exposure dose to the rectal mucosa should be measured as accurately as possible. With this in mind, a new dosimeter using lithium fluoride in small capsules which were inserted in a flexible catheter in tandem was developed. This "dosimetry catheter," inserted in the rectum for variable periods of time, gave measurements which were compared with those of a rigid scintillation probe that is in general clinical use. It has been demonstrated that the dose rates obtained with the scintillation probe and those obtained by the flexible dosimetry catheter are approximately the same to the level of the vaginal radium. At that point, the dosimetry catheter curves posteriorly following the normal anatomic contour of the rectosigmoid, and the exposure doses recorded are considerably less than the ones obtained by the rigid scintillation probe. Further careful studies of the actual dose range of tolerance to the rectal mucosa, as recorded by the rectal dosimetry catheter, may lead in the future to the better understanding of the dose range tolerance of the rectal mucosa to radium and radium-equivalent material.

J. J. Sheldon, M.D.
Department of Radiology
Jackson Memorial Hospital
Miami, Florida 33136

We would like to thank our Physics Department, especially Louis Katchis who built the lithium fluoride read-out system. Our thanks also to Al Hancock, our dosimetrist, whose help and suggestions in calibrating our instruments were indispensable.

REFERENCES

1. Baily, N. A., Norman, A., and Hilbert, J. W. Direct reading intracavitary dosimeter for use in radium therapy. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1967, *99*, 382–386.
2. Bruno, F. P., and Mauderli, W. Intracavitary radiation probe. *Brit. J. Radiol.*, 1966, *39*, 870–872.
3. Cameron, J. R., Zimmerman, D., Kenney, G., *et al.* Thermoluminescent radiation dosimetry utilizing LiF. *Health Physics*, 1964, *10*, 25–29.
4. Chau, P. M., Fletcher, G. H., Rutledge, F. N., and Dodd, G. D., Jr. Complications in high dose whole pelvis irradiation in female pelvic cancer. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1962, *87*, 22–40.
5. Deeley, T. J. Routine measurement of rectal dose in treatment of carcinoma of cervix by radium. *J. Fac. Radiologists*, 1954, *5*, 289–291.
6. Fletcher, G. H., Brown, T. C., and Rutledge, F. N. Clinical significance of rectal and bladder dose measurements in radium therapy of cancer of uterine cervix. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1958, *79*, 421–450.
7. Fletcher, G. H., Wall, J. A., Bloedorn, F. G., Shalek, R. J., and Wootton, P. Direct measurements and isodose calculations in radium therapy of carcinoma of cervix. *Radiology*, 1953, *61*, 885–902.
8. Karzmark, C. J., White, J., and Fowler, J. F. Lithium fluoride thermoluminescence dosimetry. *Phys. Med. & Biol.*, 1964, *9*, 273–286.
9. Kottmeier, H. L., and Gray, M. J. Rectal and bladder injuries in relation to radiation dosage in carcinoma of cervix. *Am. J. Obst. & Gynec.*, 1961, *82*, 74–82.
10. Million, R. R., Mauderli, W., and Bruno, F. P. Modification of technic for bladder and rectal measurements in carcinoma of cervix. *Radiology*, 1966, *86*, 921–925.
11. Todd, T. F. Rectal ulceration following irradiation treatment of carcinoma of cervix uteri: pseudo-carcinoma of rectum (Hunterian Lecture). *Surg., Gynec. & Obst.*, 1938, *67*, 617–631.
12. Turner, R. C., and Newbery, S. P. Probe test direct reading dosage-rate meter. *Brit. J. Radiol.*, 1950, *23*, 424–429.
13. Worton, R. G., and Holloway, A. F. Lithium fluoride thermoluminescence dosimetry. *Radiology*, 1966, *87*, 938–943.
14. Zilliacus, H. Dosimeter for preventing radiation injuries to rectum during treatment of carcinoma of uterus with radium. *Acta radiol.*, 1947, *28*, 790–795.

ENHANCEMENT OF X-RAY EFFECTS ON THE SMALL INTESTINAL EPITHELIUM OF DOGS BY ACTINOMYCIN D*

By JOSEPH P. CONCANNON, M.D., ROY E. SUMMERS, M.S., JOHN KING, D.V.M., PH.D.,† GEORGE TCHERKOW, B.S.,‡ CHRISTINE COLE, PH.B., *and* EDWARD ROGOW, M.D.§
PITTSBURGH, PENNSYLVANIA

THERE has been, in the last few decades, a major increase in the use of chemotherapeutic agents combined with ionizing radiations in the treatment of patients with malignant disease. Radiation therapists have been hopeful that such a combination might result in an enhancement of the radiation effects on tumors, without a corresponding increase in the radioresponsiveness of the normal adjacent tissues. Several excellent review articles on this subject have been published in recent years.[2,21,32,40,45,46]

The use of Actinomycin D combined with radiotherapy has been studied by many investigators.[1,3,5–7,9–13,16–18,20,24,28,29,36,38,41,42,43] Some studies have indicated that Actinomycin D combined with external radiation therapy has resulted in either enhanced regression of tumor masses, or has produced longer lasting beneficial effects in patients. It has also been claimed that certain neoplasms, such as malignant melanoma[6] and some notoriously radiation resistant sarcomas[36] have shown a favorable response to the combined treatment.

A review of the literature failed to provide convincing evidence that the use of Actinomycin D will potentiate the effects of ionizing radiations on neoplasms in humans. Altman[1] believed that he had observed such an effect in 2 patients with metastatic Wilms' tumors in whom the radiation treatment and Actinomycin D were given concomitantly. Keidan[20] stated that Actinomycin D had an effect either of its own or in potentiating the radiation effects on tumor tissue in a few of his patients who had received a low dose of radiation. Sutow[42] felt that the combination of Actinomycin D and radiation had brought about a more prolonged suppression of metastatic disease than that obtained with either radiation or drug alone. Others[28,43] have claimed that the effects of the two agents on tumors are additive rather than synergistic. Tan *et al.*,[43] although believing that the effects of the combined treatment were additive in the treatment of some tumors, found no evidence that Actinomycin D sensitized radiation resistant neoplasms to x-ray therapy.

The value of Actinomycin D combined with radiation therapy in the treatment of patients with Wilms' tumor has been disputed. Reiquam *et al.*,[38] and Maier and Harshaw[31] were unable to demonstrate improved survival rates in patients with Wilms' tumor by the addition of Actinomycin D to the therapeutic regimen of surgery and radiation treatment previously in use. Maier[31a] later stated that the use of actinomycin D, added to surgery and radiotherapy, had improved survival of patients with Stage III Wilms' tumor.

Considerable attention has been given in the literature to the uniqueness of the increased skin reaction which occurred in patients when the radiation was combined with Actinomycin D. Farber *et al.*[12] noted markedly increased x-ray effects on the skin when the combined treatment was

* Presented at the Fiftieth Annual Meeting of the American Radium Society, Miami Beach, Florida, April 7–11, 1968.
From the Division of Radiation Therapy, Department of Radiology, Allegheny General Hospital, Pittsburgh, Pennsylvania.
This investigation was supported in part by research grant T-346 from the American Cancer Society and in part by clinical research grant 1P02-CA-10438 from the National Cancer Institute, National Institutes of Health, U. S. Public Health Service.
† Fellow, Carnegie-Mellon University.
‡ Predoctoral Clinical Research Fellow, training grant T01-CA-05187—National Cancer Institute, National Institutes of Health, U. S. Public Health Service.
§ Postdoctoral Clinical Research Fellow, training grant T01-CA-05187—National Cancer Institute, National Institutes of Health, U. S. Public Health Service.

used. This phenomenon has been documented by many others. D'Angio *et al.*[6] stated that 350 r skin dose combined with Actinomycin D produced an erythema in the irradiated area comparable to that produced by 1,200 r without the drug.

Less attention has been given to the possibility of increased radiation responsiveness of other normal tissues included in the treatment volume when radiation is combined with the use of this chemotherapeutic agent. Howard[17] reported the occurrence of an acute intussception of the lower ileum in a patient receiving radiation therapy who had completed a course of Actinomycin D a few weeks prior to initiation of the radiation treatment. The resected bowel in the region of the apex of the intussception displayed several swollen areas with central ulceration. The appearance of this disease pattern at least 22 days after completion of Actinomycin D therapy and during x-ray treatment to the abdomen suggests to us that the combination of treatment may have produced an enhanced effect on the small intestine.

Knobler[22] described the death of an infant, due to pancytopenia and an exudative enterocolitis involving the entire small and large intestine, following a course of Actinomycin D (75 μg./kg. of body weight in 5 days) combined with radiation therapy (1,800 r tumor dose to the entire abdomen in 9 treatments over a 13 day period).

Keidan[20] stated that the risk of radiation pneumonitis may be greater when Actinomycin D is combined with radiation treatment. He believed that 2 of his patients treated by combination of the drug and radiation had developed radiation pneumonitis although autopsy examination was not obtained. The technical aspects of the radiation treatment given these patients were not detailed in his report. It is possible that, if these patients had radiation pneumonitis, it could have been due solely to the effects of radiation. Fatal pneumonitis has been reported with radiation doses as low as 2,500 r to the whole of both lungs.[34]

Keidan also suggested that Actinomycin D may potentiate the effects of ionizing radiation on the kidney, thereby increasing the risk of radiation nephritis. Renal biopsy revealed evidence of radiation nephritis in 1 of his patients who had received a tumor dose of 2,500 r at the level of the kidney in 22 treatments in conjunction with intravenous administration of Actinomycin D. Radiation nephritis, however, has been reported[4,25] due to radiation alone, with doses as low as 2,300 r to the whole of both kidneys in less than 5 weeks. It is difficult, therefore, to ascribe the radiation nephritis in this child as due solely to an increased effect of radiation caused by administration of Actinomycin D during the course of the radiation treatment.

Sagerman[39] reported radiation nephritis in a child who had received a total tumor dose of 2,370 rads to the kidney in 42 days in combination with Actinomycin D therapy. He speculated that the kidney may have been unduly radiosensitive because of an increased mitotic rate of the cells in the remaining kidney following contralateral nephrectomy. Our analysis of his data led us to believe that the possibility of radiation nephritis in this patient, resulting from an increased effect of radiation on renal tissue due to the concomitant use of Actinomycin D, has not been entirely excluded.

Howard[17] believed that he had observed potentiation of x-ray effects on the liver in 2 patients who had received Actinomycin D. It is difficult to accept these patients as proven cases of "radiation hepatitis," due to the combination of the effects of Actinomycin D and radiation treatment, since the details of the radiation treatment were not described. Ingold *et al.*[19] have described "radiation hepatitis" in patients receiving radiation alone at dose levels as low as 3,800 r to the entire liver.

The paucity of information in the literature on the possible potentiation of x-ray effects on various normal organs and tissues led us to design and initiate several animal investigations. The experiments reported here deal with the effect of Actinomycin D alone, x-radiation alone, and Actinomycin D combined with radiation, on the intestinal epithelium of the dog.

Table I

SCHEDULED MID-LINE ABDOMINAL X-RAY DOSE IN R TO BE FRACTIONATED INTO 12 EQUAL TREATMENTS

Actinomycin D	No Radiation	1,900	2,500	3,100
No Actinomycin D	3	5	5	5
10 μg./kg./day for 5 successive days	6	3	3	3

METHODS

Thirty-three male thoroughbred beagles were randomly assigned to the experimental groups shown in Table I. Two dogs in each of the radiation only groups and three dogs in the Actinomycin D only group were added for the purpose of autopsy comparisons and were to be sacrificed at times similar to those dying of the combined treatment. Twenty-four additional thoroughbred beagles were randomly assigned to experimental groups in a succeeding investigation to provide data at lower radiation dose levels (Table II).

The radiation was given with a Westinghouse 250 kv. constant potential apparatus, half value layer of 2.0 mm. Cu, 50 cm. focus skin distance, utilizing paired opposing lateral portals measuring 12×10 cm^2. The radiation portals were centered on the lowest ribs and extended caudally to approximately the level of the iliac crests. The indicated mid-line radiation doses were scheduled to be given in equal increments for 12 consecutive days. The treatment was given at the rate of 48 r per minute, measured on the skin. The treatments were monitored by a Siemens' integral dose rate meter. The x-ray treatments were given between 8 and 10 A.M. each day.

Actinomycin D dissolved in physiologic saline was given intravenously (10 μg./kg. body weight/day) to those animals scheduled to receive such treatment. The administration of the drug was initiated on Day 4 of the radiation treatment and was continued through Day 8. The drug was given 16 hours prior to the scheduled x-ray treatment of the following day.

The animals were caged separately. They were fed once daily on Friskies Mix and given water *ad libitum*.

All animals were examined daily and weighed on Days 1 and 9. The animals assigned to the groups listed in Table I were studied with serial white blood cell counts, platelet counts and hemoglobin determinations. Serial determinations of serum values for chlorides, sodium, potassium, inorganic phosphorus, calcium, total protein, glutamic-oxalacetic transaminase, lactic acid dehydrogenase, and blood urea nitrogen were obtained daily in the first few weeks of the investigation and less often thereafter. The stools were examined daily for blood prior to the determination of rectal temperatures. Blood cultures were obtained prior to death.

The animals assigned to the groups listed in Table II were studied with serial white blood cell, platelet, reticulocyte and differential counts. Bone marrow aspirates were

Table II

SCHEDULED MID-LINE ABDOMINAL X-RAY DOSE IN R TO BE FRACTIONATED INTO 12 EQUAL TREATMENTS

Actinomycin D	No Radiation	1,100	1,500	1,900
No Actinomycin D	3	3	3	3
10 μg./kg./day for 5 successive days	3	3	3	3

Table III

TOXICITY OF ACTINOMYCIN D GIVEN INTRAVENOUSLY TO MONGREL DOGS OBSERVED FOR 14 DAYS AFTER FINAL INJECTION

Daily Dose (μg./kg.)	Number of Daily Doses	Total Dose (μg./kg.)	Mortality	Day of Death after Final Injection
10.0	10	100	2/2	1, 1
7.5	10	75	2/3	1, 2
5.0	10	50	0/3	—
10.0	6	60	1/3	1

Table IV

NUMBER OF ANIMALS DYING OF TREATMENT AND TOTAL NUMBER OF ANIMALS IN EXPERIMENTAL GROUPS

Actinomycin D	Mid-line Abdominal X-ray Dose in r*					
	No Radiation	1,100	1,500	1,900	2,500	3,100
No Actinomycin D	0/3	0/3	0/3	0/6	0/3	0/3
10 μg./kg./day for 5 doses	0/6	0/3	0/3	4/6	2/3	3/3

* Refers to doses designated in experimental protocol.

obtained prior to treatment and on Day 11 of the x-radiation. Serial hemoglobin, plasma prothrombin and clotting time determinations were performed. The biochemical studies performed on animals assigned to groups listed in Table II, were similar to those performed on animals in groups listed in Table I.

At autopsy sections obtained from organs were fixed and prepared for microscopic examination.

RESULTS

Actinomycin D was shown, in preliminary toxicity studies, to be more toxic to dogs than to humans on a μg./kg. body weight basis. Table III indicates the results of these studies. The fatally intoxicated animals had lethargy, anorexia and bloody diarrhea prior to death. Bloody diarrhea was not seen in animals surviving to sacrifice 14 days after completion of Actinomycin D treatment.

Table V

ACTUAL RADIATION DOSES RECEIVED BY ANIMALS TREATED WITH ACTINOMYCIN D AND RADIATION WHO DIED AND ANIMALS ADDED FOR SACRIFICE PURPOSES

Protocol Designated Dose (r)	Experimental Group	Sacrifice Group
1,900	1,424	1,425
	1,583	
	1,583	1,741
	1,741	
2,500	2,083	1,875
	2,083	2,291
3,100	2,583	
	2,583	2,841
	2,583	2,325

All animals in the radiation only treatment groups received their scheduled doses of radiation. Nine of the 12 animals scheduled to receive 1,900, 2,500, and 3,100 r combined with Actinomycin D died between the ninth and the eleventh day of the x-ray treatment (Table IV). The radiation doses received by the animals dying of the combined treatment are shown in Table V. The radiation doses received by the animals in the 1,900, 2,500, and 3,100 r groups, who were added to the investigation for the purpose of autopsy comparisons, are also shown in Table V.

The treated dogs generally ate and drank less than the control non-treated animals. Anorexia was most marked in the animals receiving the combined treatment, and these animals, after the third injection of Actinomycin D, refused to take food, taking only small quantities of water. The animals in the combined treatment groups were the only animals to develop bloody diarrhea.

The control non-treated animals showed no change in weight on Day 9 of the radiation period. Most animals in the treatment groups lost weight, although variations in average weight loss among various treatment groups were not statistically significant.

Significant differences in elevations in rectal temperature between control non-treated animals and treated animals were not observed. Six animals in the combined

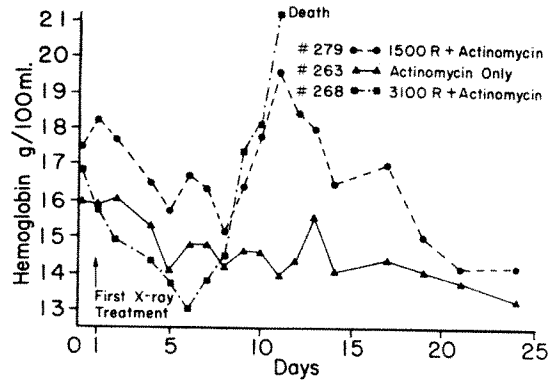


FIG. 1. Characteristic increase in hemoglobin concentration in animals dying of the combined treatment. Animal 279 had return of hemoglobin concentration to control animal levels prior to sacrifice.

treatment groups (Table 1), however, had a marked temperature depression at least one day prior to death.

HEMATOLOGIC AND BIOCHEMICAL EFFECTS

Significant differences in the platelet and white blood cell counts were not observed between treated and non-treated animals. More than half the animals, including some non-treated animals developed depression of their hemoglobin levels, due to daily bleeding for biochemical and hematologic studies. The 9 animals in the combined treatment groups who died showed a similar depression in hemoglobin level until just a few days prior to death, when evidence of hemal concentration developed (Fig. 1). The hemal concentration observed was most likely secondary to failure to ingest adequate amounts of fluid, diarrhea and the shock-like syndrome that these animals developed.

Hypochloremia (Fig. 2) was observed in 8 of 12 animals in the combined treatment groups scheduled to receive 1,900 r or more, while 1 of 6 animals in the combined treatment groups scheduled to receive less than 1,900 r had depression of serum chlorides. The serum chlorides in those animals dying acutely varied between 60–90 mEq/liter (normal 105–110 mEq/liter). Two animals with low serum chlorides who survived, had partial recovery of chlorides prior to sacrifice. Hypochloremia was not observed in animals of the other treatment groups.

Hyponatremia (Fig. 3) developed in 3 of the animals in the combined treatment groups. Animal 251, a survivor in a combined treatment group, had the lowest post-treatment values for serum sodium, 110 mEq/liter (normal 140–150 mEq/liter). Evidence of recovery in this animal prior to sacrifice was not observed.

Thirteen animals in the combined treatment groups showed an increase in serum inorganic phosphorus to 7.2–19.6 mg. per cent (normal 4–6 mg. per cent). Four animals in this group had return of serum phosphorus to normal by the eleventh

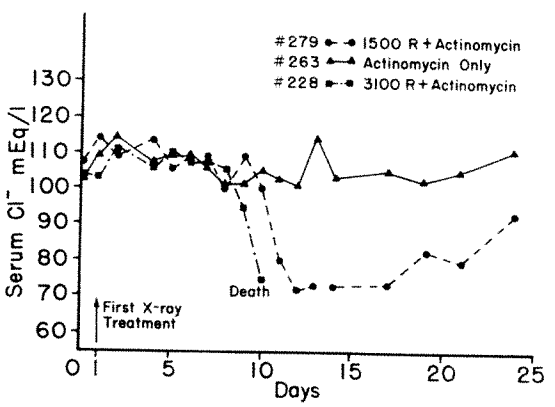


FIG. 2. Characteristic decrease in serum chloride levels in animals dying of the combined treatment. Animal 279 had partial recovery of serum chloride prior to sacrifice.

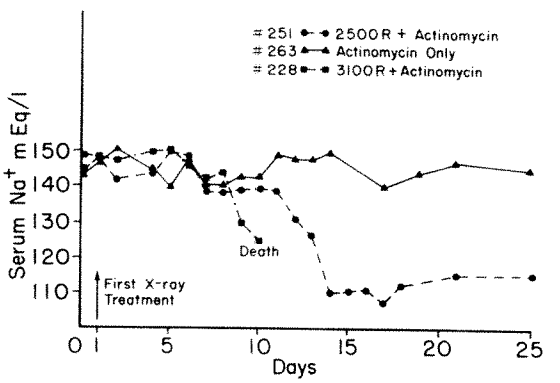


FIG. 3. Decrease in serum sodium levels noted in a few animals in the combined treatment groups.

treatment day. Four of 9 animals receiving Actinomycin D only, also had an elevation of serum phosphorus (7.5–9.3 mg. per cent). Figure 4 illustrates the characteristic changes in serum phosphorus.

Four of the 9 animals in the combined treatment groups (Table 1) had elevation of plasma protein levels to 7–8 mg. per cent (normal 5–6 mg. per cent). Animal 251 (2,500 r and Actinomycin D) had reversion of plasma protein to normal levels prior to sacrifice (Fig. 5).

Serum levels for potassium, calcium, serum glutamic oxalacetic transaminase and lactic dehydrogenase were unaffected by any treatment. Blood urea nitrogen was elevated in only a few animals in the combined treatment groups prior to death. The blood cultures prior to death were negative for pathogenic organisms.

A consistent depression of lymphocytes was observed only in those animals receiving Actinomycin D, whether or not they received radiation treatment. Reticulocyte counts were not altered by any form of treatment. Bone marrow examination prior to death demonstrated probable bone marrow depression in 5 of the animals who received either Actinomycin D alone or in combination with radiation treatment. One animal (1,900 r+Actinomycin D) had evidence of an aplastic bone marrow just prior to death. Plasma prothrombin times and clotting times were unaffected by any treatment.

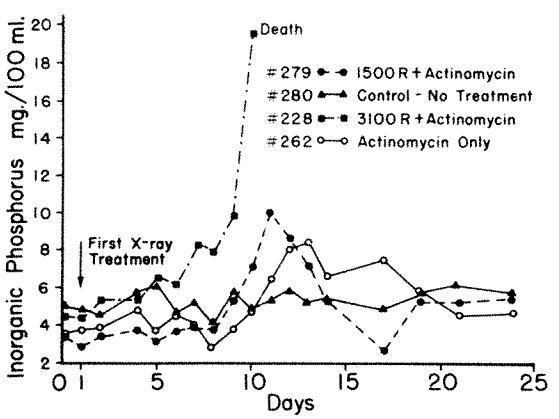


FIG. 4. Characteristic increase in serum inorganic phosphorus levels in animals receiving either Actinomycin D alone or Actinomycin D combined with x-ray treatment.

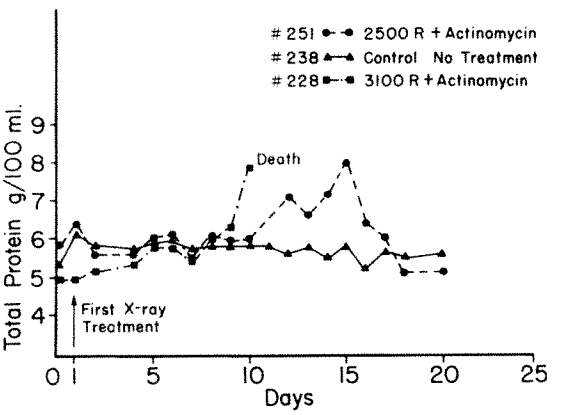


FIG. 5. Increase in serum total protein concentration observed in nearly half the animals receiving the combined treatment.

PATHOLOGIC EFFECTS

Significant gross autopsy findings were limited to the small intestines of those animals in the combined radiation and Actinomycin D treatment groups which died acutely. The gastrointestinal tract was empty in these animals other than for a large amount of hemolyzed blood. The entire duodenum and a major portion of the jejunum were invariably involved by the pathologic process. Abnormal loops of jejunum and ileum were observed, sometimes interspersed between normal appearing segments of bowel. The involved segments of small bowel varied from a dark erythematous appearance to a purplish hue indistinguishable from that of gangrene of the bowel. The Peyer's patches were almost completely destroyed. The mucosa in many areas appeared to be abnormally thin.

Histologically the characteristic lesion in those animals which died acutely, was a marked denudation and atrophy of the mucosa. The number of crypts were markedly reduced. The cells in the remaining crypts were often pleomorphic in appearance with large and bizarre cells. Edema and vascular dilatation of the mu-



FIG. 6. Photomicrograph of duodenum of Animal 228 (3,100 r group + Actinomycin D). Despite postmortem autolytic changes, loss of villi and dilated crypts with intraluminal debris can be observed. Marked submucosal congestion is present. (Hematoxylin and eosin; × 48.)

cosa was observed in most animals. Figures 6 and 7 are photomicrographs of the duodenum of Animal 228 (3,100 r+Actinomycin D).

DISCUSSION

The effects of whole body and abdominal irradiation on the gastrointestinal tract of experimental animals have been extensively studied. The histologic changes in the small intestine after lethal doses of radiation have been reported [26,27] as cessation of mitosis, karyorrhexis, and pyknosis of the basal cells of the crypts of Lieberkühn with the occasional production of abnormal and bizarre cells. Cessation of mitosis, if prolonged, leads to denudation of the villi. Sublethal doses of radiation result in a temporary reduction of crypt cell population but recovery soon takes place. The critical point in survival is whether or not cell production is effectively resumed in time to prevent complete denudation of the villi.

Lethally irradiated animals become dehydrated and the hematocrit rises sharply. There is a major loss of electrolytes from the body in the terminal phase of the radiation induced gastrointestinal syndrome.

Studies of the toxic effects of Actinomycin D on the gastrointestinal tract of various animal species have been described by a number of investigators. Hackmann[15] reported mitotic inhibition of cells in the crypts of Lieberkühn as well as degeneration and desquamation of the intestinal epithelium. Philips and associates[35] also stated that the small and large intestines of rats were extensively damaged by Actinomycin D in high doses. They described swelling of cells, loss of nuclear polarity, ectasia and karyorrhexis in the basal regions of the small intestine.

They also described in detail the toxicity of Actinomycin D in dogs. The fatally intoxicated animals and most of the survivors had bloody diarrhea. Severe hypochloremia and hyponatremia were the only consistent serum biochemical abnormalities

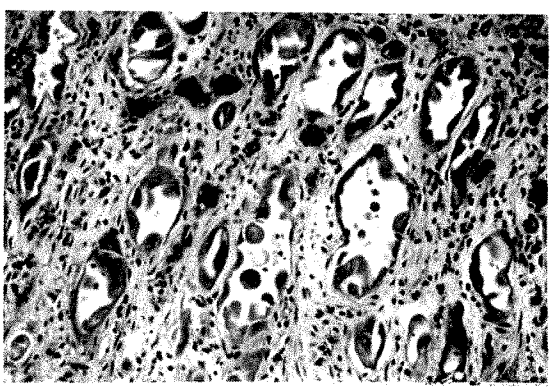


FIG. 7. Photomicrograph of duodenum of Animal 228 (3,100 r group + Actinomycin D). There is a marked reduction in number of crypts. The crypt cells are large, bizarre and pleomorphic. Debris are seen in many crypts. (Hematoxylin and eosin; × 192.)

that could be identified. The 5 dogs they autopsied showed severe histologic changes in both small and large intestine, consisting of swelling and atypia of the epithelial nuclei, glandular ectasia, clubbing of villi, and moderate but significant atrophy and congestion.

Clinical experience suggests that Actinomycin D may produce similar effects on the gastrointestinal mucosa of man. The toxic effects of the drug on the gastrointestinal tract in man have been described as nausea, vomiting and diarrhea which may be severe. Occasional abdominal pain after Actinomycin D has been reported. The observation of severe changes in the buccal mucosa and extensive ulcerative stomatitis is not uncommon.

Maddock *et al.*[30] indicated that enhancement of x-ray effects of Actinomycin D can be demonstrated in normal tissues of mice other than the skin. They stated that, when Actinomycin D at doses that have no observable effect was added to a relatively innocuous dose of x-ray, a greater degree of injury was observed in both hematopoietic and small intestinal tissue. The authors concluded that "Such a combination when the target is the small intestine, may result in the death of the animal."

Despite the striking similarities in the clinical syndromes and histologic appearance of the small bowel in dogs, produced by either high dose intravenous Actinomycin D alone or high dose irradiation alone, the mechanisms of action are probably different. There is a substantial body of evidence to indicate that the effects of ionizing radiations on cells result either directly from the interaction of the radiation with DNA, or indirectly from the interaction of DNA with highly reactive radiation produced chemical compounds. Actinomycins, on the other hand, are known to interfere with the synthesis of mRNA and protein by binding to the guanine residues of DNA, displacing the RNA polymerase enzyme from its normal binding site.[37]

The mechanism of action of the enhanced response of the intestinal epithelium to ionizing radiations produced by the concomitant administration of Actinomycin D is not clear. Knock[23] has speculated that Actinomycin D may potentiate radiation effects by the generation of free radicals which then attack DNA. White and Dearman [47] have documented the generation of free radicals from Streptonigrin which has an aminoquinone grouping similar to the Actinomycins.

Elkind *et al.*[8] in split radiation dose experiments with Chinese hamster cells, demonstrated repair of sublethal damage in the survivors of the first radiation dose. They observed, in a later investigation using the same system that Actinomycin D significantly affected repair. They stated that at least one locus of sublethal x-ray damage involves DNA in relationship to its molecular environment (nucleic acid replicases, histone and non-histone proteins, etc.) which is re-established at least functionally in repair. They suggested that the presence of Actinomycin D during the repair process may either interfere with the reassociation or make ineffective sites which are repaired.

Griem and Ranniger's[14] data on the production of dysplastic changes in mouse anagen hairs with the combination of Actinomycin D and x-radiation suggest another possible mechanism for the enhanced effect on normal tissues observed after the use of the combined treatment. They observed increased production of dysplastic hair when 400 r of x-radiation was given 4 and 16 hours after the administration of Actinomycin D (150 μg./kg. body weight). Definite inhibition in production of dysplastic hairs was observed when the x-radiation was given 1, 12 and 36 hours after the drug. These data suggest that the use of the drug may have partially synchronized the cell population of the hair follicle. Mueller and Kajiwara[33] demonstrated marked inhibition of mitosis when HeLa cells in synchronized culture were treated with Actinomycin D in the S

period. Tobey *et al.*[44] further demonstrated in Chinese hamster ovary cell suspensions, synchronized by thymidine treatment, that Actinomycin D produced a block 1.9 hours before completion of division.

The possibility exists that the increased damage to the intestinal epithelium noted in this investigation, when Actinomycin D was combined with x-radiation, may be due to a combination of several different mechanisms. Actinomycin D by itself in the dose used (10 μg./kg. of body weight for 5 successive days), although not productive of significant clinical or histologic changes, is not far removed from that dose of Actinomycin D which produces severe gross histologic epithelial changes in the small intestine resulting in the death of the animal. It is possible that Actinomycin D, in the dose used in this investigation, either reduced the number of viable crypt cells or inflicted a sublethal injury on many of these cells. The effects of ionizing radiation on a reduced number of viable cells or cells sublethally damaged by the Actinomycin D could be a prominent factor in the production of the increased damage. The data of Elkind *et al.*[8] would certainly suggest that another major cause of the increased effect would be the Actinomycin D inhibition of repair of sublethal damage in previously irradiated cells. Finally, Griem and Ranniger's[14] data on production of dysplastic hairs is suggestive that Actinomycin D in our investigation produced partial synchrony of the crypt cells resulting in a larger fraction of the cells being in a radiosensitive phase of the cell cycle, 16 hours after administration of the drug, when the x-radiation was given.

Attention is drawn to the inherent dangers of combining radiation with Actinomycin D in the treatment of patients with intra-abdominal neoplasms. The appearance of moderate to severe gastrointestinal symptoms, when such combined treatment is used, should be the signal for immediate interruption of treatment.

SUMMARY

1. The combination of Actinomycin D and irradiation of the upper portion of the abdomen of dogs, in doses which, by themselves, produce no significant clinical, histologic or biochemical abnormalities, resulted in the death of 9 of 12 animals scheduled to receive between 1,900 and 3,100 r. The actual radiation doses received by these animals were lower than those scheduled (1,424–2,583 r) since many animals died prior to completion of the proposed x-radiation. The cause of death was undoubtedly related to the severe changes produced in the epithelium of the small intestine following the combined treatment of Actinomycin D and x-radiation.

2. Marked depression of serum chlorides was observed in more than half of the animals in the group which received Actinomycin D and x-radiation. Hyponatremia was observed in only a few animals in the combined treatment groups. The elevation of serum phosphorus observed in many of the animals in the various treatment groups appeared to be related to the administration of Actinomycin D rather than due to the effects of the combined treatment. Bone marrow depression and the depression in lymphocytes observed in this investigation also appeared to be related primarily to the use of the drug.

3. Mechanisms of action for the enhanced response of the small intestinal epithelium to x-radiation and Actinomycin D treatment are postulated.

4. The appearance of severe gastrointestinal symptoms in patients receiving combined Actinomycin D and x-radiation treatment to the abdomen should be an indication for immediate interruption of treatment.

Joseph P. Concannon, M.D.
Division of Radiation Therapy
Department of Radiology
Allegheny General Hospital
320 East North Avenue
Pittsburgh, Pennsylvania 15212

We are grateful to Marvin Slifkin, Ph.D. of the Singer Memorial Research Institute who was responsible for the bacteriologic studies performed. We are also grateful to Mr. William Lau for his meticulous care of the animals used in this investigation.

REFERENCES

1. Altman, D. H. Actinomycin D and roentgen-ray therapy in treatment of metastatic Wilms' tumor. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1961, *86*, 673–681.
2. Berry, R. J. Modification of radiation effects. *Radiol. Clin. North America*, 1965, *3*, 249–258.
3. Colebatch, J. H., Howard, R., Williams, A. L., Kurrle, G. R., and Clark, A. C. L. Results of Actinomycin D therapy for Wilm's tumour. *Acta Unio internat. contra cancrum*, 1964, *20*, 491–492.
4. Concannon, J. P., Summers, R. E., Brewer, R., Weil, C., and Hayeslip, D. High oxygen tension and radiation effect on kidney. *Radiology*, 1964, *82*, 508–519.
5. D'Angio, G. J. Clinical and biologic studies of Actinomycin D and roentgen irradiation. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1962, *87*, 106–109.
6. D'Angio, G. J., Farber, S., and Maddock, C. L. Potentiation of x-ray effects of Actinomycin D. *Radiology*, 1959, *73*, 175–177.
7. D'Angio, G. J. Laboratory and clinical observations with combined Actinomycin D and x-radiation. *Laval méd.*, 1963, *34*, 137–139.
8. Elkind, M. M., Moses, W. B., and Sutton-Gilbert, H. Radiation response of mammalian cells grown in culture. VI. Protein, DNA and RNA inhibition during repair of x-ray damage. *Radiation Res.*, 1967, *31*, 156–173.
9. Farber, S. Chemotherapy in treatment of leukemia and Wilms' tumor. *J.A.M.A.*, 1966, *198*, 826–836.
10. Farber, S. Clinical and biological studies with Actinomycin. In: Ciba Foundation Symposium on Amino Acids and Peptides with Antimetabolic Activity. Edited by G. E. W. Wolstenholme and C. M. O'Connor. Little, Brown & Company, Boston, 1958, pp. 138–145.
11. Farber, S., D'Angio, G. J., Evans, A., and Mitus, A. Clinical studies of Actinomycin D with special reference to Wilms' tumor in children. *Ann. New York Acad. Sc.*, 1960, *89*, 421–424.
12. Farber, S., Toch, R., Sears, E. M., and Pinkel D. Advances in chemotherapy of cancer in man. In: Advances in Cancer Research. Volume IV. Edited by J. P. Greenstein and A. Haddow. Academic Press, New York, 1956, pp. 1–71.
13. Fernbach, D. J., and Martyn, D. T. Role of D actinomycin in improved survival of children with Wilms' tumor. *J.A.M.A.*, 1966, *195*, 1005–1009.
14. Griem, M. L., and Ranniger, K. Modification of radiation effect on hair roots of mouse by Actinomycin. *Radiation Res.*, 1962, *17*, 92–100.
15. Hackmann, C. Untersuchungen über den Einfluss des Sanamycins (Actinomycin C) auf tierische Organe: Milz, Thymus, Lymphknoten, Nebennieren und Keimdrüsen. *Ztschr. Krebsforsch.*, 1954, *60*, 250–255.
16. Hope, J. W., Borns, P. F., and Koop, C. E. Diagnosis and treatment of neuroblastoma and embryoma of kidney. *Radiol. Clin. North America*, 1963, *1*, 593–619.
17. Howard, R. Actinomycin D in Wilm's tumour: treatment of lung metastases. *Arch. Dis. Childhood*, 1965, *40*, 200–202.
18. Howard, R. Neuroblastoma (Wilms' tumour): improved prognosis with Actinomycin D. *M. J. Australia*, 1964, *2*, 141–142.
19. Ingold, J. A., Reed, G. B., Kaplan, H. S., and Bagshaw, M. A. Radiation hepatitis. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1965, *93*, 200–208.
20. Keidan, S. E. Actinomycin D in treatment of cancer in children. *Brit. J. Surg.*, 1966, *53*, 614–618.
21. Kligerman, M. M. Present status of combined radiation therapy and chemotherapy. In: Progress in Radiation Therapy. Edited by F. Buschke. Grune & Stratton, Inc., New York, 1965, pp. 183–199.
22. Knobler, M. Personal communication.
23. Knock, F. E. Anticancer Agents. Charles C Thomas, Publisher, Springfield, Ill., 1967.
24. Koop, C. E. Current management of nephroblastoma and neuroblastoma. *Am. J. Surg.*, 1964, *107*, 497–501.
25. Kunkler, P. B., Farr, R. F., and Luxton, R. W. Limit of renal tolerance to x-rays: investigation into renal damage occurring following treatment of tumors of testis by abdominal baths. *Brit. J. Radiol.*, 1952, *25*, 190–201.
26. Lesher, S., and Bauman, J. Progress report of studies concerned with damage, repair and recovery in proliferative cells of mouse duodenal crypt. To be published.
27. Lesher, S., and Vogel, H. H. Comparative histological study of duodenal damage produced by fission neutrons and Co^{60} gamma rays. *Radiation Res.*, 1958, *9*, 560–571.
28. Liebner, E. J. Actinomycin D and radiation

therapy. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1962, *87*, 94–105.

29. LIEBNER, E. J., KIRKPATRICK, G. P., and ROSENTHAL, I. M. Various childhood tumors: treatment with Actinomycin D and x-ray therapy. *Illinois M. J.*, 1962, *121*, 531–537.
30. MADDOCK, C. L., D'ANGIO, G. J., FARBER, S., and HANDLER, A. H. Biological studies of Actinomycin D. *Ann. New York Acad. Sc.*, 1960, *89*, 386–398.
31. MAIER, J. G., and HARSHAW, W. G. Treatment and prognosis in Wilms' tumor. *Cancer*, 1967, *20*, 96–102. a. MAIER, J. G. Personal communication, 1968.
32. MITCHELL, J. S. A review of clinical and laboratory studies of radiosensitizers in radiotherapy. In: Progress in Biochemical Pharmacology. Volume I. Edited by R. Paoletti and R. Vertua. Butterworth & Co. Ltd., Washington, 1965, pp. 335–351.
33. MUELLER, G. C., and KAJIWARA, K. Actinomycin D and p-fluorophenylalanine, inhibitors of nuclear replication in HeLa cells. *Biochim. et biophys. acta*, 1966, *119*, 557–565.
34. NEWTON, K. A. Total thoracic irradiation combined with intravenous injection of autogenous marrow. *Clin. Radiol.*, 1960, *11*, 14–21.
35. PHILIPS, F. S., SCHWARTZ, H. S., STERNBERG, S. S., and TAN, C. T. Toxicity of Actinomycin D. *Ann. New York Acad. Sc.*, 1960, *89*, 348–360.
36. RANNIGER, K., and GRIEM, M. L. Modification of radiation response of tumors by actinomycin D: clinical evaluation. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1966, *96*, 147–149.
37. REICH. E. Actinomycin: correlation of structure and function of its complexes with purines and DNA. *Science*, 1964, *143*, 684–689.
38. REIQUAM, C. W., PROSPER, J. C., AKERS, D. R., ALLEN, R. P., and BEATTY, E. C. Wilms' tumors: study of 42 cases at Denver Children's Hospital (1943–1964). *Rocky Mountain M. J.*, 1965, *62*, 43–49.
39. SAGERMAN, R. H. Radiation nephritis. *J. Urol.*, 1964, *91*, 332–336.
40. SCOTTE DOGETT, R. L., BAGSHAW, M. A., and KAPLAN, H. S. Combined therapy using chemotherapeutic agents and radiotherapy. In: Modern Trends in Radiotherapy. Volume I. Edited by T. J. Deeley and C. A. P. Wood. Appleton-Century-Crofts, New York, 1967, pp. 107–131.
41. SHAW, R. K., MOORE, E. W., MUELLER, P. S., FREI, E., III, and WATKIN, D. M. Effect of Actinomycin D on childhood neoplasms. *A.M.A. Am. J. Dis. Child.*, 1960, *99*, 628–635.
42. SUTOW, W. W. Effective chemotherapy in children with Wilms' tumor. *South. M. J.*, 1967, *60*, 254–256.
43. TAN, C. T., DARGEON, H. W., and BURCHENAL, J. H. Effect of Actinomycin D on cancer in childhood. *Pediatrics*, 1959, *24*, 544–561.
44. TOBEY, R. A., PETERSEN, D. F., ANDERSON, E. C., and PUCK, T. T. Life cycle analysis of mammalian cells. III. Inhibition of division in Chinese hamster cells by Puromycin and Actinomycin. *Biophys. J.*, 1966, *6*, 567–580.
45. VERMUND, H., and GOLLIN, F. F. Mechanisms of action of radiotherapy and chemotherapeutic adjuvants. *Cancer*, 1968, *21*, 58–76.
46. VERMUND, H. Experimental approaches to radiotherapy. In: The Biological Basis of Radiation Therapy. Edited by E. E. Schwartz. J. B. Lippincott Company, Philadelphia, 1966, pp. 518–591.
47. WHITE, J. R., and DEARMAN, H. H. Generation of free radicals from phenazine methosulphate, streptonigrin, and rubiflavin in bacterial suspensions. *Proc. Nat. Acad. Sc. U.S.A.*, 1965, *54*, 887–891.

RESPONSE TO RADIATION THERAPY OF OSSEOUS LESIONS DETECTED ON RADIOISOTOPE BONE SCANS*

By SHELDON BAUM, M.D.,† JAMES H. DAVENPORT, M.D.,‡
and LAWRENCE SILVER, M.D.†
JAMAICA, NEW YORK

IT IS now well established that osseous metastases may be recognized on radioisotope bone scans prior to the time they can be visualized on roentgenograms.[2] The identification of these lesions on bone scans is often helpful in determining sites for treatment with irradiation.[5]

In a group of 13 patients with known primary neoplasms arising from several sites, radiotherapy was directed at osseous metastases detected on Sr^{85} bone scans but which were not seen on roentgenograms. It is the purpose of this paper to report the response of these "hidden" lesions to radiation therapy for symptomatic relief of pain.

MATERIALS AND METHODS

Bone scanning was performed 72 hours after the intravenous administration of 125 μc of strontium nitrate (Sr^{85}). For scanning of the vertebral column or pelvis, a cathartic was given the night before scanning and an enema was given 2 hours prior to the scanning to cleanse the bowel of the radioactive material. Scanning was done at random on 1 of 2 rectilinear scanners, utilizing either a 3 inch or 5 inch sodium iodide crystal. With the former, a 19 hole collimator was used, and with the latter, a coarse focusing 85 hole collimator was used. The maximum scale deflection was 1,500–2,000 counts per minute.

Radiotherapy was administered to 12 patients by means of filtered 250 kv. roentgen rays of a half-value layer of 3.0 mm. Cu, with a target skin distance of 50 cm. Treatment was given to a single field directly over the lesion. The daily tumor dose ranged from 100–400 rads and the total tumor dose from 1,600–2,400 rads (Table 1). One patient was treated with cobalt 60 teletherapy.

Each patient had a known primary tumor and a bone scan positive for skeletal metastases. In each instance, the Sr^{85} bone scanning had been performed only when the roentgenogram showed no osseous metastases in the area in question. The primary neoplasms arose from a number of sites (5 from lung, 2 from cervix and 1 each from esophagus, pancreas, colon, breast, lymphatic system and soft tissue).

RESULTS

The response of the patients to radiotherapy was considered to be good, fair or unchanged in regard to the symptomatic relief of pain from the metastatic bone lesions.

Good response: Relief of pain for at least 2 months after therapy.

Fair response: Relief of pain for at least 4 weeks but less than 2 months after therapy.

Unchanged: No improvement in patient's discomfort.

A summary of the clinical data is presented in Table 1.

PATIENTS TREATED WITH 250 KV. ROENTGEN RAYS

Good response. Nine patients had a good response with symptomatic relief of pain lasting from 2 months to at least 23 months. Three patients who expired from their underlying disease (Patients No. 2, 9 and 12) had no return of the localized pain for which they were treated at the times of their deaths.

* Presented at the Fiftieth Annual Meeting of the American Radium Society, Miami Beach, Florida, April 7–11, 1968.
From the Long Island Jewish Hospital, Queens Hospital Center Affiliation, Jamaica, New York.
† Department of Nuclear Medicine.
‡ Department of Radiation Therapy.

TABLE I

SUMMARY OF CLINICAL DATA

Patient No.	Age	Sex	Primary Neoplasm	Site of Metastases Identified on Scan	Apparatus	Half-Value Layer	Total Tumor Dose (r)	Dose per Treatment (r)	No. of Treatments	Duration of Treatments (wk.)	Result
1	29	F	Cervix; squamous cell carcinoma, Stage II	Sacrum	250 kv.	3.0 mm. Cu	2,000	200	10	2	Fair—6 wk.
2	73	M	Lung; oat cell carcinoma	Lower lumbar vertebrae	250 kv.	3.0 mm. Cu	2,000	400	5	$1\frac{2}{3}$	Good—2 mo. (expired)
3	41	F	Lung; epidermoid carcinoma	Lower dorsal and upper lumbar vertebrae	250 kv.	3.0 mm. Cu	1,600	400	4	$1\frac{1}{3}$	Fair—6 wk.
4	42	M	Lung; epidermoid carcinoma	Right iliac crest and acetabulum	250 kv.	3.0 mm. Cu	2,000	200	10	2	Good—at least 6 mo.
5	36	F	Breast; infiltrating duct cell carcinoma	Seventh cervical and first thoracic vertebrae	250 kv.	3.0 mm. Cu	2,400	400	6	2	Good—at least 23 mo.
				Right ilium	250 kv.	3.0 mm. Cu	2,000	100	10	2	Good—at least 11 mo.
				Lumbar spine	250 kv.	3.0 mm. Cu	2,400	200	12	$2\frac{1}{2}$	Good—at least 9 mo.
6	50	M	Esophagus; epidermoid carcinoma	Left scapula	250 kv.	3.0 mm. Cu	2,000	200	10	2	Good—8 mo.
7	65	F	Pancreas; adenocarcinoma	Lumbosacral spine	250 kv.	3.0 mm. Cu	2,000	200	10	2	Good—at least 6 mo.
8	48	M	Lung; epidermoid carcinoma	Right rib cage, anteriorly	250 kv.	3.0 mm. Cu	2,400	200	12	$2\frac{1}{2}$	Fair—4 wk.
9	42	F	Ascending colon; adenocarcinoma	Lumbosacral spine	250 kv.	3.0 mm. Cu	1,600	400	4	4 da.	Good—3 mo. (expired)
10	26	F	Retroperitoneal; lipomyxosarcoma	Right ilium	Co^{60}		3,000	200	15	3	Poor—unchanged
11	57	F	Lung; epidermoid carcinoma	Left sacrum and left ilium	250 kv.	3.0 mm. Cu	2,400	200	12	$2\frac{2}{5}$	Good—9 mo. (lost to follow-up)
12	55	F	Cervix; squamous cell carcinoma, Stage II	Right ilium	250 kv.	3.0 mm. Cu	2,000	100	20	4	Good—5 mo. (expired)
13	73	F	Lymphosarcoma	Lumbosacral spine	250 kv.	3.0 mm. Cu	1,540	220	7	$2\frac{1}{2}$	Good—3 mo.

Three patients (Patients No. 4, 5 and 7) are still being followed and have had no recurrence of pain. One of these (Patient No. 12) has had radiotherapy on 3 successive occasions for bone metastases as they developed and in each instance had a good result.

Fair response. Three patients had a fair response with symptomatic relief of pain lasting 4 weeks in 1 and 6 weeks in the other 2 patients.

PATIENTS TREATED WITH Co^{60} TELETHERAPY

Only 1 patient (Patient No. 10) was treated with Co^{60} teletherapy and her pain was unchanged after therapy. She had a

lipomyxosarcoma with extension into the right ilium. The primary neoplasm and the extension into bone were treated simultaneously.

The following is a representative case report.

REPORT OF A CASE

Case 5. This 36 year old female had a left radical mastectomy in February, 1965, for an infiltrating duct cell carcinoma of the breast with regional lymph node metastases. Postoperatively, she received 6,000 rads of Co^{60} teletherapy. In January, 1966, she developed right scapular and lower cervical spine pain but the roentgenograms were negative (Fig. 1). A radioisotope bone scan performed 72 hours after the intravenous administration of 125 μc of Sr^{85} showed increased activity in C-7 and D-1 (Fig. 2) and was consistent with metastatic involvement. She received 2,400 rads to this area during a period of 2 weeks with disappearance of her pain. She continued to do well until October, 1966, when she complained of right hip pain. Roentgenograms were negative (Fig. 3) but a radioisotope bone scan demonstrated evidence of metastases in the right ilium, including the acetabulum (Fig. 4). Following a course of 2,000 rads to the involved area in the ilium over a period of 2 weeks, she was asymptomatic. She again continued to do well until April, 1967, when low back pain developed. Roentgenograms of the dorsal and lumbar vertebrae continued to show no metastases but a Sr^{85} bone scan revealed increased uptake in D-12 and the lumbar vertebrae (Fig. 5). A course of 2,400 rads to the region D-12–L-5 over a $1\frac{1}{2}$ week period resulted in relief of her painful symptoms. She is now asymptomatic, has resumed her clerical occupation and is being treated with cytoxan 150 mg./day.

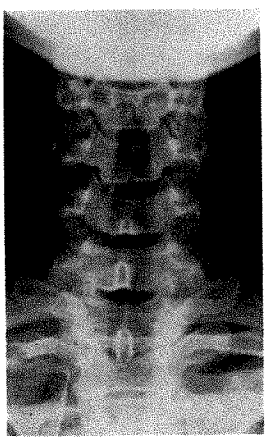


Fig. 1. *January, 1966*: Roentgenogram of the cervical spine showing no evidence of metastases.

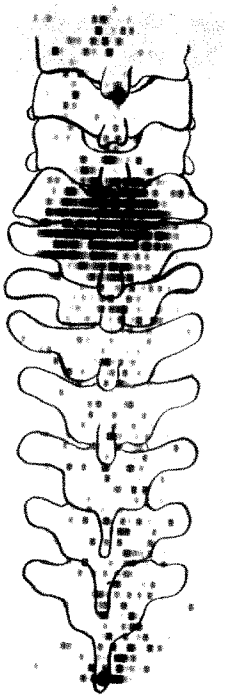


Fig. 2. Radiostrontium bone scan same time as Figure 1 shows increased radioactivity in C-7 and D-1, indicating metastases.

DISCUSSION

It has been demonstrated that increased calcium deposition occurs at the sites of bone metastases, both osteoblastic and osteolytic.[3] This increased calcium deposition commences long before sufficient bone destruction enables these bone lesions to be visualized on roentgenograms.

Strontium behaves in the body in a manner similar to that of calcium.[1] When radioactive strontium is administered intravenously, it becomes deposited, like calcium, in increased amounts in the areas surrounding bone metastases. Thus, Sr^{85} scans may detect these lesions at an early stage, sometimes many months prior to their recognition on roentgenograms.[4]

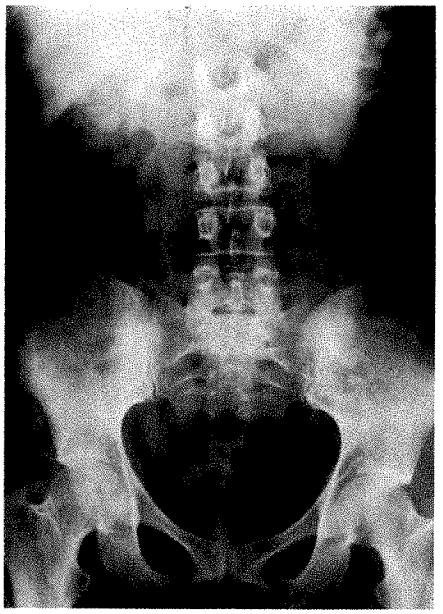


FIG. 3. *October, 1966*: Roentgenogram showing no evidence of metastases in the lumbosacral spine and pelvis.

In each of the cases reported in this paper, localized pain in a patient with a known malignancy was the reason for bone scanning. In each case, the skeletal metastasis was identified on the scan but could not be seen on the roentgenogram. The primary tumors arose from a number of different sites (cervix, breast, lung, esophagus, pancreas, colon, lymphatic system and soft tissue).

The osseous metastases were treated with deep roentgen therapy in 12 patients and, in each, the initial symptomatic improvement was dramatic. The over-all response from this mode of therapy was considered good in 9 patients and fair in 3. The single patient who experienced no beneficial effect from roentgen therapy was treated with Co^{60} teletherapy for direct extension of a lipomyxosarcoma into the ilium.

The precise changes effected by radiotherapy to the developing metastases have not yet been explained. These early lesions are highly responsive to irradiation, inasmuch as symptomatic relief of pain is concerned.

Bone scanning appeared to be a valuable adjunct in reducing the disability in patients with known primary neoplasms. At the first instance of significant bone pain, Sr^{85} bone scannings were performed if the roentgenogram was negative. If positive, irradiation was promptly directed to the site

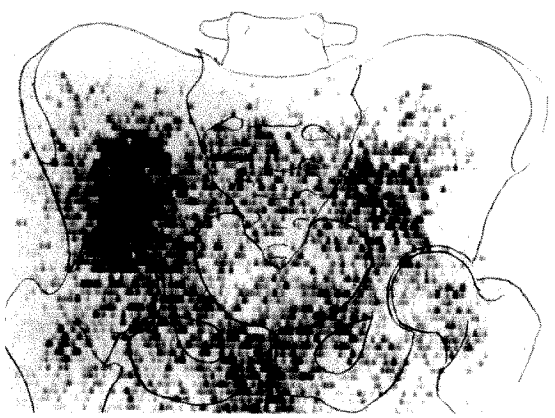


FIG. 4. A Sr^{85} bone scan at the same time as Figure 3 shows an area of increased radioactivity in the right ilium, including the acetabulum, consistent with a metastatic lesion.



FIG. 5. *April, 1967*: Bone scan showing increased activity in D-12 and the lumbar vertebrae. Scanning of D-2–11 did not indicate increased radioactivity.

of involvement. In this manner, patients, symptomatic for relatively short periods could return to normal duties rapidly.

In patients with known skeletal metastases, Sr^{85} bone scans detected additional lesions not seen on roentgenograms. Prompt radiation therapy to these areas of involvement resulted in marked symptomatic improvement with no undue lag period necessary for confirmation by roentgenograms.

From this experience, it appears that patients with known primary tumors should have radioisotope bone scanning if significant bone pain is present, metastases are suspected, and roentgenograms are negative. The good response of these lesions to radiotherapy justifies their search through isotopic methods.

SUMMARY

In a group of 13 patients with known primary neoplasms, radiotherapy for symptomatic relief of pain was directed at osseous metastases detected on Sr^{85} bone scans but which were not seen on roentgenograms. The response was considered to be good in 9 patients, fair in 3 and poor in 1.

It is probable that these early lesions, detected on bone scans before sufficient bone destruction has occurred to enable them to be seen on roentgenograms, are more sensitive to radiotherapy than fully visualized metastases.

Sheldon Baum, M.D.
Department of Radiology
New York Medical College
Fifth Avenue at 106th Street
New York, New York 10029

The scannings were performed by Ruth Lane, Norma deJunco and Virginia Mastis. Veronica Mather assisted in patient treatment. Yetta Lemberg assisted in collecting and assembling the follow-up data and preparing the manuscript.

REFERENCES

1. Charkes, N. D., and Sklaroff, D. M. Detection of occult metastases to bone by photoscanning with radioisotopes of strontium. In: Progress in Clinical Cancer. Volume I. Edited by I. Ariel. Grune & Stratton, Inc., New York, 1965, pp. 235–257.
2. Charkes, N. D., Sklaroff, D. M., and Young, I. Critical analysis of strontium bone scanning for detection of metastatic cancer. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1966, *96*, 647–656.
3. Corey, K. R., Kenny, P., Greenberg, E., Pazianos, A., Pearson, O. H., and Laughlin, J. S. Use of calcium 47 in diagnostic studies of patients with bone lesions. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1961, *85*, 955–975.
4. Papworth, M. P., and Andrews, J. T. Localization of bone disease with radiostrontium. *J. Nuclear Med.*, 1967, *8*, 723–734.
5. Spencer, R., Herbert, R., Rish, M. W., and Little, W. A. Bone scanning with ^{85}Sr, ^{87m}Sr and ^{18}F. *Brit. J. Radiol.*, 1967, *40*, 641–654.

PAROSTEAL OSTEOSARCOMA*

By DONALD A. WOLFEL, M.D.,† *and* PETER R. CARTER, B.A.‡

THE parosteal osteosarcoma is an uncommon and atypical bone-forming malignant neoplasm which possesses distinctive clinical and roentgenologic characteristics. Recognition and differentiation of this tumor from the usual osteosarcoma of medullary cavity origin is vital, since a strikingly improved prognosis can be anticipated if proper treatment is instituted. The following 3 patients, correctly diagnosed and treated in the past 7 years, exemplify the salient features of this pathologic process.

REPORT OF CASES

CASE I. This 34 year old Negro female was first seen in March, 1960 because of a painless, gradually enlarging mass on the dorsum of the right wrist of 8 months' duration. A history of trauma could not be elicited. Roentgen studies of the wrist revealed a multilobulated dense osseous neoplasm surrounding the distal diaphysis and metaphysis of the radius (Fig. 1, *A–C*). The tumor did not appear to invade the medullary cavity although there was slight pressure erosion of the lateral aspect of the distal ulna. A roentgenologic diagnosis of parosteal osteosarcoma was rendered. After normal chest roentgenography and skeletal survey, an open biopsy was performed. The pathologic diagnosis of the submitted tissue was osteosarcoma of the parosteal type. Two weeks later, a right supracondylar amputation was carried out and a hard, white, lobulated, 7–8 cm. mass involving the distal radius was found. The radial cortical bone was intact. The final microscopic diagnosis was parosteal osteosarcoma, reaffirming the biopsy diagnosis. Seven years later, the patient is living and well without evidence of metastases.

CASE II. This 49 year old white female was aware of a slowly growing mass in the right popliteal fossa for at least 10 years. She had been seen by physicians elsewhere during that period with mixed and varied opinions concerning the nature and proper therapy of the lesion. At the time of admission (1962) rather marked, nontender enlargement of the right knee was apparent. Roentgenograms of the knee demonstrated a large osseous tumor encircling the distal one-third of the right femur, with roentgenologic features characteristic of parosteal osteosarcoma (Fig. 2, *A–C*). Amputation was recommended, and, after 2 months of patient procrastination, accomplished. The tumor measured 13 cm. in length, 1–4 cm. in thickness, and extended 2 cm. into the soft tissues. The microscopic diagnosis was parosteal osteosarcoma. The patient is well $4\frac{1}{2}$ years later without evidence of metastases.

CASE III. This 36 year old white male suffered a minor injury of the left knee 3 weeks prior to admission (1963). Because of fullness in his popliteal space, he was referred for radiologic study. Roentgenograms revealed a typical parosteal osteosarcoma arising from the posterior surface of the distal metaphyseal area of the femur (Fig. 3, *A* and *B*). Two open biopsies were performed, and a histologic diagnosis of parosteal osteosarcoma rendered locally was subsequently confirmed by Dr. H. L. Jaffe. A mid-thigh amputation was performed and the diagnosis substantiated by final histologic study. Marrow invasion was not present. The patient is well, without metastatic disease, 4 years later.

DISCUSSION

Parosteal osteosarcoma was first regarded as a distinct entity by Geschickter and Copeland[4] in 1951, although undoubtedly cases prior to this date did exist and were relegated to the category of "osteogenic sarcoma" or "osteoma." These authors emphasized the malignant capabilities of the tumor in describing a 25 per cent incidence of pulmonary metastases. Shortly thereafter, Dwinnell, Dahlin and Ghormley[3] confirmed these findings in their series and suggested the more meaningful name

* From Department of Radiology, The University of Maryland Hospital, Baltimore, Maryland.
† Associate Professor of Radiology, The University of New Mexico School of Medicine, Albuquerque, New Mexico.
‡ Clinical Clerk in Radiology, The University of New Mexico School of Medicine, Albuquerque, New Mexico.

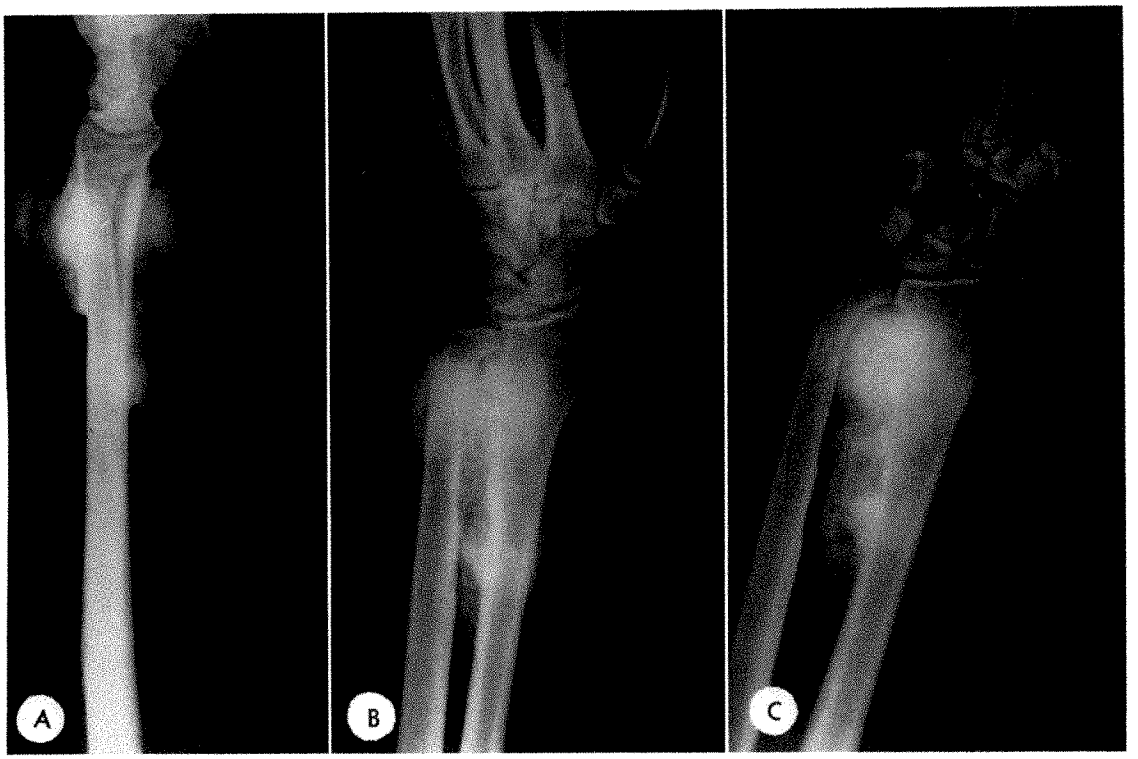


Fig. 1. Case 1. (*A–C*) Parosteal osteosarcoma arising in an unusual location adjacent to the radius. Note the intact cortex of the radius and the poorly ossified periphery of the tumor, representing areas of predominant cartilaginous and fibrous tissue.

of "parosteal osteogenic sarcoma" for the neoplasm.[3] Since these initial observations, approximately 90 cases (including this report) have been described in the literature and from this material certain unique and identifying characteristics of the tumor stand out.[1–6,9–15]

The parosteal osteosarcoma is rather uncommon with an incidence estimated at 3 to 4 per cent of all bone forming neoplasms.[11] The disease affects individuals in an age group somewhat older than the conventional osteosarcoma, with an average age of 30 years reported at the time of detection. No sex predilection is apparent. At least two-thirds of these tumors have been found in relation to the femur, usually the popliteal surface of its distal end. Other long bones have also been implicated as primary sites; specifically, the tibia, humerus, fibula, phalanges, ulna and radius. (Case 1 in this series is only the second reported instance of the sarcoma arising adjacent to the radius.) Bones other than those of the appendicular skeleton are seldom involved, although one tumor has been described originating from the cervical spine, scapula and mandible respectively.[6,14] Since the neoplasm is believed to be derived from the periosteum or parosteal connective tissues and since, in general, it is rather indolent and slow-growing, the tumor at the time of detection is usually large and bulky, projecting into the soft tissues of the extremity. The cortex of the underlying bone is, in most instances, intact, without extension of the disease into the medullary cavity and this is the basic diagnostic feature that distinguishes this entity from the more common osteosarcoma of medullary origin. Exceptionally, the tumor may be of sufficient duration and agressiveness that marrow cavity invasion has occurred at the time of detection; this has been associated with a poor prognostic index and with the ultimate appearance of metastatic lesions. The

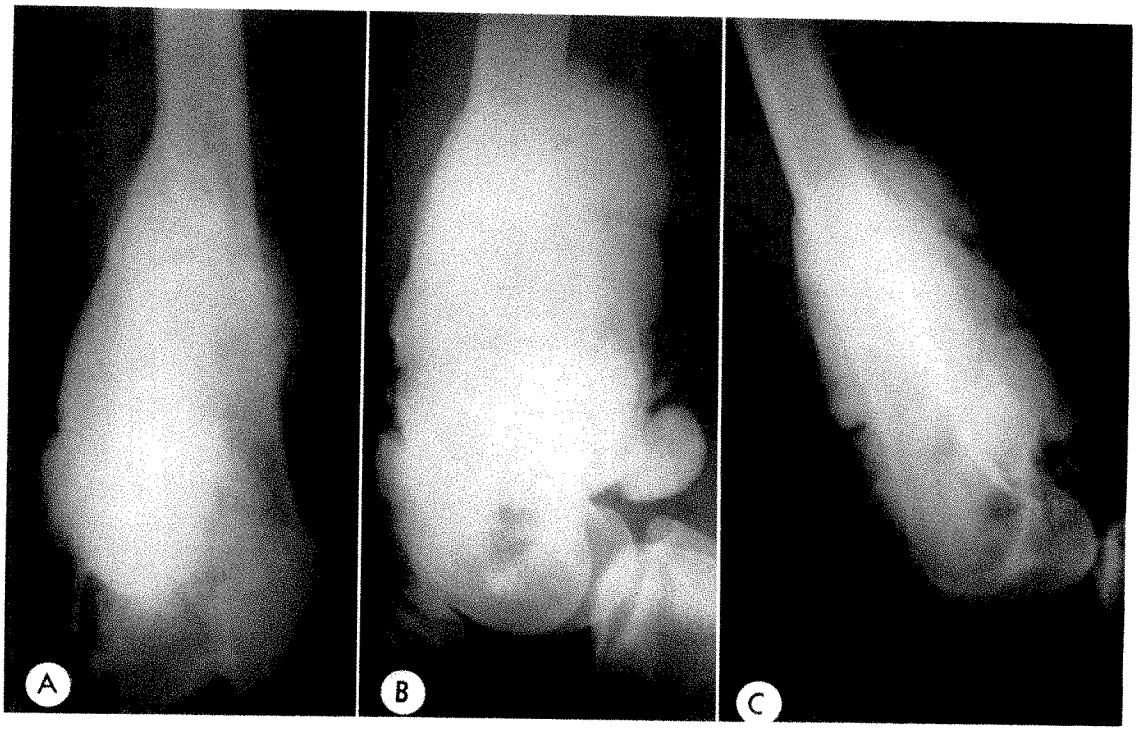


FIG. 2. Case II. (*A–C*) Typical densely ossified parosteal osteosarcoma arising in its most common location—the posterior surface of the distal third of the femur. Roentgenogram of the amputated specimen (*C*) better defines the intact cortex with lack of medullary invasion.

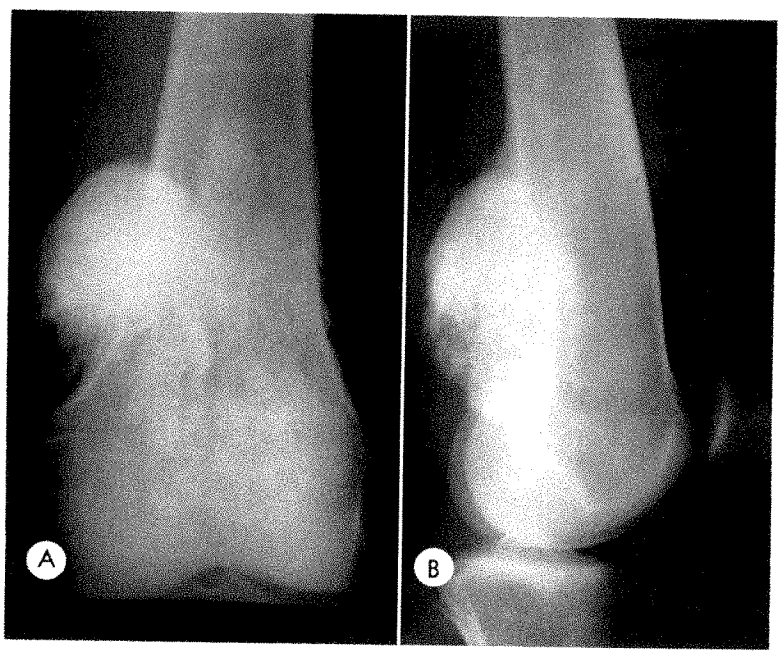


FIG. 3. Case III. (*A* and *B*) A characteristic parosteal osteosarcoma situated in its conventional location. The less ossified lower quadrant of the tumor is the optimal area to biopsy for obtaining histologic proof of malignancy.

patient may be totally unaware that he is harboring a neoplasm (as Case III) or the presence of a slowly-growing, nontender extremity mass may have been known for 10 to 20 years (as Case II). The tumor has a propensity for recurrence following attempted local excision—an often difficult surgical task in view of the circumferential relationship of the neoplasm to the adjacent bone. Generally, the agressiveness of the sarcoma appears to increase with repeated attempted excisions, judging from a correlation with reported mortalities, and such efforts, although well intended, may be complicated eventually by dissemination of the disease to the lungs.[1,4,12]

The roentgenologic features of the parosteal sarcoma are sufficiently characteristic to allow for a diagnosis at the time of initial detection, in most instances. The tumor arises in relation to the metaphysis of a long bone and, in a majority of cases, the posterior surface of the distal third of the femur is involved. The neoplasm is large and lobulated with sharply defined margins. It is densely opaque, with the denseness being greater at its base than its periphery. The density of the tumor often tends to obscure the underlying cortex and medullary cavity and laminagraphy may be required to show the usual integrity of these structures or, uncommonly, their compromise. As indicated previously circumferential distribution of the neoplasm about the underlying bone is a salient roentgenologic observation. At times, a radiolucent "line of cleavage" may be detected between the base of the tumor and the intact cortex. The usual roentgenologic manifestations of a bone sarcoma—*i.e.*, periosteal reaction or elevation, cortical destruction, medullary cavity invasion, Codman's triangle—are lacking in the vast majority of instances. Myositis ossificans, osteochondroma, and subperiosteal hematoma are the lesions which have been reported to simulate parosteal osteosarcoma from a roentgenologic standpoint, but this differential diagnostic problem would seem to apply to the tumor in its earlier, rather than later, stages.[7,15] Little information is available concerning the natural history of the tumor or its appearance in the initial stages, so that the differential diagnosis of an "early" parosteal osteosarcoma seems more academic than practical.

The gross appearance of the neoplasm has been mentioned in the previous discussion. The tumor is composed basically of dense mature bone, with the periphery often possessing areas of cartilaginous and fibrous tissue. The more malignant of these tumors tend to have less osseous tissue, this pathologic feature correlating at times with the relative density demonstrated by roentgenologic studies.[7] Microscopic evaluation of the neoplasm has been quite difficult and has, on occasions, led to less than optimal therapy. The evidence of malignancy is subtle and is to be found in the sarcomatous spindle cell stroma in the intratrabecular spaces. Large areas of the tumor may appear quite benign histologically, so that identification of the lesion may be difficult and, at times, impossible by multiple biopsy technique. The tendency in previous years has been to underestimate the malignant potential of the neoplasm histologically, and this has led directly to attempts at local excision—an often inadequate therapeutic procedure.[7,8]

The appropriate surgical treatment for the patient harboring a parosteal osteosarcoma must be evaluated with the knowledge of the potential of this tumor to recur and to metastasize. Initial efforts should be directed toward obtaining histologic proof of the sarcoma by biopsy. Parenthetically, biopsy attempts should not be carried to the extreme and if the roentgenologic findings are typical, correct surgical therapy should be undertaken despite the inability to demonstrate convincing malignant change by histologic means. If the neoplasm is small, local *en bloc* excision may be possible. Should a subsequent local recurrence develop, then it would appear that amputation of the

extremity is indicated, since evidence does point to a more guarded prognosis with repeated local excisions. In the majority of instances, amputation seems to be the optimal treatment since frequently the tumor cannot be adequately excised. The 20–25 per cent mortality rate reported in the literature reflects, in the main, inadequate initial surgical therapy.[4,15] A small number of these tumors present with early medullary cavity invasion and a grave prognosis, but this fraction is considerably smaller than the reported mortality. The survival rate in more recent years is better than those reported earlier, indicating a greater awareness of the malignant potential of the tumor by surgeons, pathologists and radiologists. With proper treatment, complete cure can be obtained in the majority of patients. In those in whom metastases appear, long periods of survival can be anticipated. An average longevity of 8–20 years for those patients succumbing to metastatic disease has been reported in the larger series.

SUMMARY

Three additional cases of parosteal osteosarcoma are reported, the details of these cases characterizing the outstanding features of this uncommon, slowly metastasizing, and often curable sarcoma. The tumor should be correctly diagnosed by its roentgenologic appearance at the time of initial examination and histologic confirmation of malignancy obtained. A decrease in the reported 25 per cent mortality of this neoplasm can be anticipated with application of proper surgical therapy, usually amputation.

Donald A. Wolfel, M.D.
Department of Radiology
University of New Mexico School of Medicine
Albuquerque, New Mexico 87106

REFERENCES

1. AAKHUS, T., EIDE, O., and STOKKE, T. Parosteal osteogenic sarcoma. *Acta radiol.*, 1960, *54*, 29–40.
2. COLEY, B. L. Atypical forms of bone sarcoma. *Bull. Hosp. Joint Dis.*, 1951, *12*, 148–173.
3. DWINNELL, L. A., DAHLIN, D. C., and GHORMLEY, R. K. Parosteal (juxtacortical) osteogenic sarcoma. *J. Bone & Joint Surg.*, 1954, *36A*, 732–744.
4. GESCHICKTER, C. F., and COPELAND, M. M. Parosteal osteoma of bone: new entity. *Ann. Surg.*, 1951, *133*, 790–807.
5. HARKESS, J. W. Parosteal osteosarcoma. *Am. Surgeon*, 1964, *30*, 730–736.
6. JACOBSON, S. A. Early juxtacortical osteosarcoma (parosteal osteoma). *J. Bone & Joint Surg.*, 1958, *40A*, 1310–1328.
7. JAFFE, H. L. Tumors and tumorous conditions bones and joints. Lea and Febiger, Philadelphia, 1958.
8. JAFFE, H. L., and SELIN, G. Tumors of bones and joints. *Bull. New York Acad. Med.*, 1951, *27*, 165–174.
9. MATHIAS, P. F., SUBRAHMANYAM, C. S. V., and RAO, B. D. P. Juxtacortical osteogenic sarcoma. *Indian J. Radiol.*, 1963, *17*, 1–4.
10. RANNIGER, K., and ALTNER, P. C. Parosteal osteoid sarcoma. *Radiology*, 1966, *86*, 648–651.
11. SAMMONS, B. P., SARKISIAN, S. S., and KREPELA, M. C. Juxtacortical osteogenic sarcoma. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1958, *79*, 592–597.
12. SCAGLIETTI, O., and CALANDRIELLO, B. Ossifying parosteal sarcoma: parosteal osteoma or juxtacortical osteogenic sarcoma. *J. Bone & Joint Surg.*, 1962, *44A*, 635–647.
13. SIRSAT, M. V., and DOCTOR, V. M. Parosteal (juxtacortical) osteogenic sarcoma: emphasis on histopathology. *J. Postgrad. Med.*, 1965, *11*, 191–197.
14. SOM, M., and PEIMER, R. Juxtacortical osteogenic sarcoma of mandible. *A.M.A. Arch. Otolaryng.*, 1961, *74*, 532–536.
15. STEVENS, G. M., PUGH, D. G., and DAHLIN, D. C. Roentgenographic recognition and differentiation of parosteal osteogenic sarcoma. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1957, *78*, 1–12.

VOL. 105, NO. 1

DEVELOPMENT OF ULTRASTRUCTURAL RADIATION INJURY*

By W. R. HENDEE, PH.D., M. A. ALDERS, B.S., *and* C. E. GARCIGA, M.D.
DENVER, COLORADO

MANY different models have been proposed for the development of cellular injury following exposure of cells and animals to ionizing radiation. In most models, changes in cell function and morphology are separated from initial radiation interactions by biochemical events which are difficult to investigate. Sequential alterations in the morphology of irradiated cells should reflect more obscure changes in cellular biochemistry. Consequently, delineation of the development of these structural changes may increase our understanding of radiation-induced biochemical alterations and our comprehension of cellular radiation injury.

Patterns of development of radiation-induced morphologic alterations are known only incompletely. This paper describes electron microscopic studies of changes in hepatic parenchymal cells from mice sacrificed 2 minutes after onset of whole body irradiation. Parenchymal cells were studied because their morphologic response to a number of toxins has been described extensively. Additionally, results of earlier work with tissue culture cells[1,2,3] implied that the endoplasmic reticulum, which parenchymal cells display in abundance, is involved intimately in the ultrastructural response of cells to irradiation.

MATERIAL AND METHOD

Female, adult mice were irradiated with Co^{60} gamma rays at a dose rate of 1,500 rads/minute. Average whole body doses ranged from 3,000 to 16,000 rads. The mice were killed by cervical dislocation from immediately to 24 hours after exposure. Tissue was extracted from the deep parenchyma of irradiated and control mice and placed immediately in gluteraldehyde-collidine fixative. By this procedure, some liver tissue was fixed a few seconds beyond 2 minutes after onset of irradiation. Methods of fixation and embedding are outlined in Table 1. Thin sections were stained with lead citrate and uranyl acetate before electron microscopic examination at 50 kv.

RESULTS

A low magnification view of a control hepatic parenchymal cell is shown in Figure 1. Mitochondria, endoplasmic reticulum and glycogen are characteristic of the liver parenchyma. The nucleus is regular in outline, with an amorphous nucleolus and chromatin typical of parenchymal cells. Membranes of the rough-surfaced endoplasmic reticulum are well-defined and possess high densities of RNP granules.

A region of a nonirradiated hepatic parenchymal cell is shown in greater detail in Figure 2. The abundance of rough-surfaced endoplasmic reticulum in parenchymal cells, and the high densities of RNP granules along the membranes, are apparent.

Changes in cell ultrastructure found immediately after exposure may provide insight into cellular events which are related closely to initial cell radiation injury. Shown in Figure 3 is a portion of a hepatocyte fixed 2 minutes after onset of irradiation to 3,000 rads. A region of cytoplasm is enveloped by electron dense membranes. The contrast of the membranes resembles that of osmiophilic, unsaturated lipid. We believe that dense membranes found in irradiated cells originate within the rough-surfaced endoplasmic reticulum.

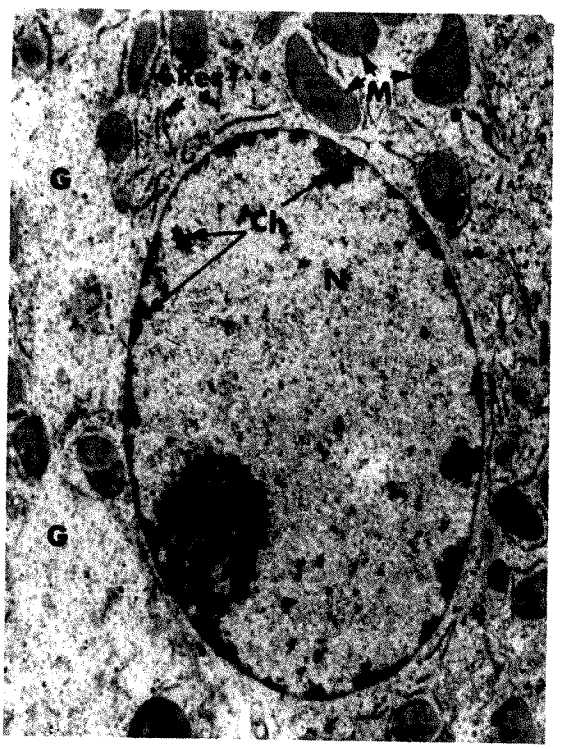
Electron dense membranes illustrated in Figure 4 appear to be continuous with structurally unaltered rough-surfaced endoplasmic reticulum. The increased density of

* Presented at the Fiftieth Annual Meeting of the American Radium Society, Miami Beach, Florida, April 7–11, 1968.
From the Department of Radiology, University of Colorado Medical Center, Denver, Colorado.

TABLE I

FIXATION-EMBEDDING PROCEDURE FOR MOUSE LIVER

Tissue	→ Gluteraldehyde-collidine +1% acrolein, pH 7.4	→ Minced tissue
		↓
Gluteraldehyde-collidine-acrolein solution, 15 to 30 minutes, 4°C.	← Collidine-OsO_4 (1:1), pH 7.4, 1 hour, 4°C.	← 2% uranyl acetate in H_2O, 30 minutes, 4°C.
		↓
Progressive Vestopal infiltration in glycolmethacrylate	→ 96% glycolmethacrylate, 12 hours	→ Progressive 4°C. dehydration in glycolmethacrylate
		↓
Three 1-hour changes and one overnight change pure Vestopal	← Initial polymerization 2,600 Å, 12 hours	← Final polymerization 60°C., 48 hours



affected membranes may reflect degradation of the lipoprotein composition of normal reticulum. The dense membranes are within a cell fixed 2 minutes after onset of exposure.

Another dense annulus is depicted in Figure 5. Altered membranes and dense annuli are found often in irradiated cells and usually are continuous with vestiges of endoplasmic reticulum. Ribosomes frequently are detached from reticulum which is continuous with dense membranes.

Shown in Figures 6, 7 and 8 are electron-dense membranous configurations which apparently originate within the rough-surfaced endoplasmic reticulum. The increased

FIG. 1. Control hepatic parenchymal cell. G = glycogen; N = nucleus; Nu = nucleolus; Ch = chromatin; M = mitochondrion; Rer = rough-surfaced endoplasmic reticulum. (Magnification ×6,900.)

electron density of affected membranes implies the presence of unsaturated lipid, resulting perhaps from structural degradation of normal reticulum. The dense membranes are within cells fixed 2 minutes following onset of irradiation to 3,000 rads. Similar electron dense membranes are observed only rarely in control cells.

DISCUSSION

Many changes are observed in the architecture of parenchymal cells from animals sacrificed a few hours after irradiation.[3,4] These alterations include dilatation of the rough-surfaced endoplasmic reticulum, distention and distortion of mitochondrial and nuclear envelopes, swelling of mitochondrial cristae, deposition of lipid within the cytoplasm and depletion of glycogen stores.



FIG. 2. Region within a control hepatic parenchymal cell, illustrating the abundance of rough-surfaced endoplasmic reticulum with high densities of RNP granules. Rer = rough-surfaced endoplasmic reticulum; M = mitochondrion; Ch = chromatin; N = nucleus. (Magnification × 7,800.)

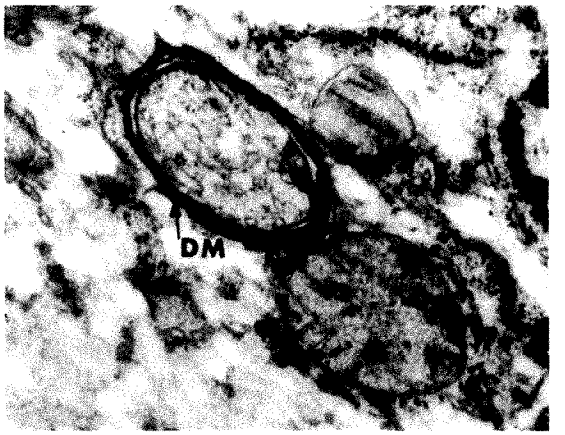


FIG. 3. Electron dense membranes within a hepatocyte fixed 2 minutes after onset of irradiation to 3,000 rads. DM = dense membranes. (Magnification × 29,000.)

Similar changes have been described during studies of the response of hepatocytes to various toxic agents, and probably repre-



FIG. 4. Continuity between dense membranes and rough-surfaced endoplasmic reticulum is apparent in this cell fixed 2 minutes after onset of exposure to 3,000 rads. DM = dense membranes; N = nucleus. (Magnification × 54,000.)

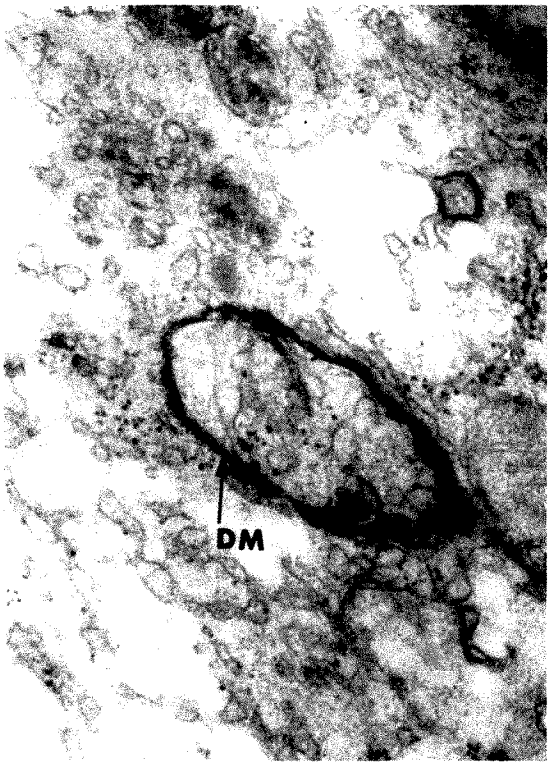


FIG. 5. The increased electron density of altered membranes in cells fixed soon after onset of exposure implies the presence of unsaturated lipid. Structural degradation of the lipoprotein composition of the endoplasmic reticulum may be responsible for the increased contrast of affected membranes. This cell was fixed 2 minutes after onset of irradiation to 3,000 rads. DM = dense membranes. (Magnification × 42,000.)

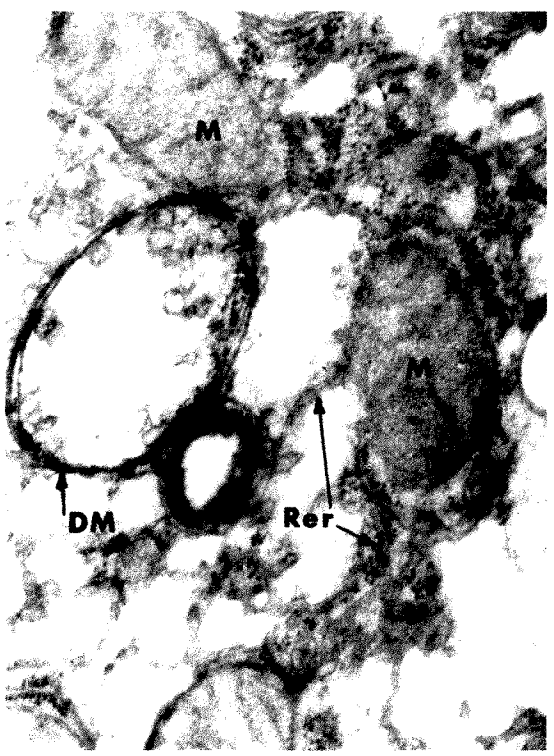


FIG. 6. Abnormal membranous configuration with increased electron density which originates within the rough-surfaced endoplasmic reticulum. This region is within a hepatic parenchymal cell fixed 2 minutes after onset of irradiation to 3,000 rads. M = mitochondrion; DM = dense membranes; Rer = rough-surfaced endoplasmic reticulum. (Magnification × 33,000.)

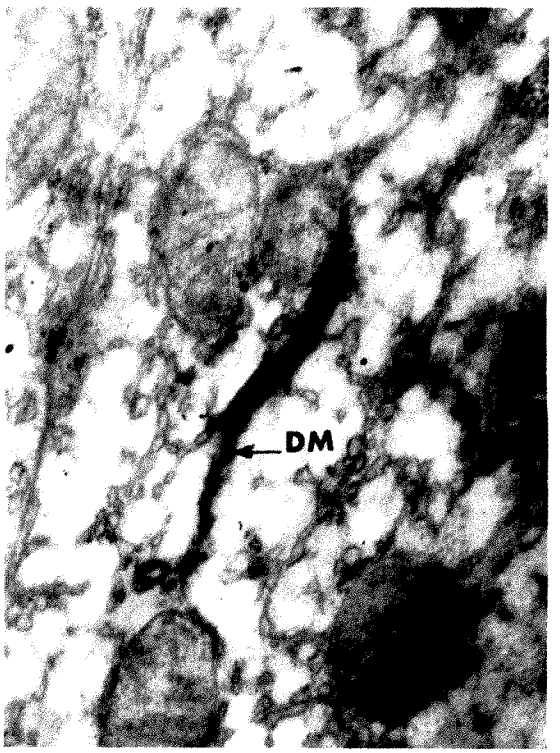


FIG. 7. Apparently degenerate endoplasmic reticulum within a hepatocyte fixed 2 minutes after onset of exposure to Co^{60} gamma rays; total dose was 3,000 rads. DM = dense membranes. (Magnification × 33,000.)

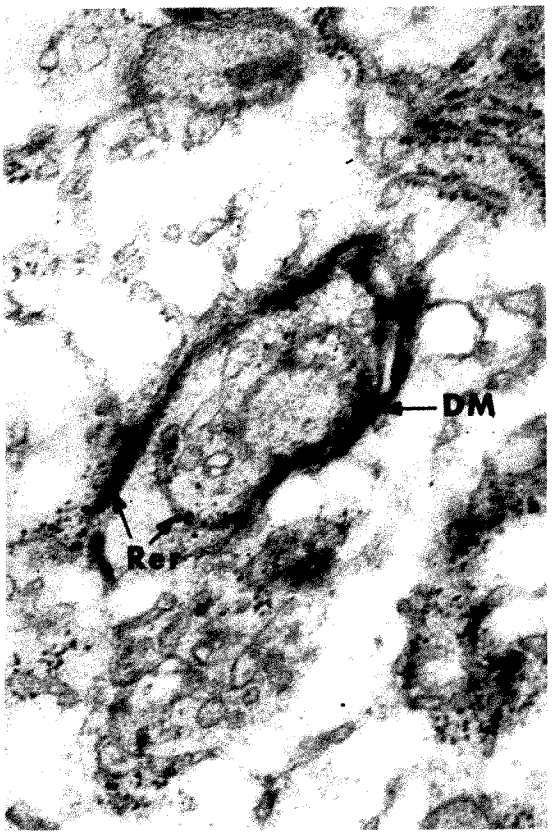


FIG. 8. Dense membranes continuous with rough-surfaced endoplasmic reticulum are observed frequently in hepatocytes fixed immediately after receipt of high radiation doses. This cell was fixed 2 minutes after onset of irradiation to 3,000 rads. DM = dense membranes. Rer = rough-surfaced endoplasmic reticulum. (Magnification ×37,000.)

sent nonspecific degenerative changes which accompany cell injury. Some of the changes, such as lipid deposition and glycogen depletion, may be related to reduced functional capability of the endoplasmic reticulum.[4]

Changes in the rough-surfaced endoplasmic reticulum similar to those occurring immediately after irradiation have not been described during studies of parenchymal cells exposed to other cytotoxic agents. We have not observed similar alterations in hepatocytes of mice injected with carbon tetrachloride. The increased electron density of affected membranes implies the presence of unsaturated lipid, resulting possibly from degradation of the lipoprotein composition of normal reticulum.

CONCLUSION

The rapid occurrence of alterations in parenchymal cells suggests a relationship between these changes and biochemical events occurring within the cell during radiation exposure. However, the frequency of occurrence of reticulum alterations decreases rapidly as the radiation dose is lowered below about 1,000 rads. Further study of these cytoplasmic abnormalities and their relationships to initial cell radiation injury is in progress.

William R. Hendee, Ph.D.
Department of Radiology
University of Colorado Medical Center
4200 East Ninth Avenue
Denver, Colorado 80220

REFERENCES

1. HENDEE, W. R., ZEBRUN, W., and BONTE, F. J. Effects of x-irradiation on fine structure of HeLa cells. *Texas Rep. Biol. & Med.*, 1963, 21, 546–557.
2. HENDEE, W. R., and ALDERS, M. Ultrastructural manifestations of cellular radiation dose. *Radiology*, 1967, *88*, 588–589.
3. HENDEE, W. R., and ALDERS, M. A. Initial radiation effects in cell ultrastructure. *Health Phys.*, 1967, *13*, 935.
4. HENDEE, W. R., and ALDERS, M. A. Ultrastructural development of radiation injury in hepatic parenchymal cells of γ-irradiated mice. *Lab. Invest.*, 1968, *18*, 151–158.

TELECOBALT SPLIT FIELD DOSIMETRY*

WITH SPECIAL REFERENCE TO CENTRAL PENUMBRAL ISODOSE SEPARATION

By RICHARD F. MOULD, M.Sc., A.INST.P.
LONDON, ENGLAND

THE radiation split field is a device by which a central portion of a treatment volume may be shielded when the adjacent parts of the volume are irradiated. Two of its applications are: (1) in irradiation of the parametria following an intracavitary radium technique for cancer of the cervix uteri; and (2) in irradiation of the cervical lymph node areas of the neck when shielding of the midline structure is necessary.

In stating dosimetry for a split field, there are 3 quantities of interest to the radiotherapist:

(i) the separation of isodose lines within the shielded zone, which will describe the lateral boundaries of the tissue volume which requires a minimal dose;
(ii) the radiation dose beneath the center of the shielded area; and
(iii) the depth doses along the central axes of the field portions adjacent to the shielded area.

It is the isodose line separation, (i), which is most difficult to estimate. The penumbra at the edge of the central shielded zone is narrower than the outside edge of an open field which has had its penumbra trimmed with a lead shield. It is therefore not possible to construct a central penumbral zone for a split field by separating 2 open field curves by a distance equal to the width of the shadow cast by the shield on the skin surface, width d' in Figure 2. The geometric edge of an untrimmed open field is defined by the 80% isodose at the Royal Marsden Hospital. The isodose separation will be sensitive to source size and position of shield with respect to the source, that is, factors which differ among existing telecobalt units. The numerical data in this paper which were obtained for a source size 1.7 cm. in diameter are, therefore, given as an example to draw attention to a method of estimating data for the split field isodose curve. Previously published data are limited to a few individual isodose curves.[1,2,5,6,7] These authors have presented dose variation behind shielded areas in telecobalt fields and have only considered square shields placed in square fields. For telecobalt units with different source sizes and source shield distances, experimental measurements similar to those described here may be carried out to determine the constants of the relationship between isodose line separation and parameters of the unit, including source skin distance (S.S.D.) and shield width.

In a recent publication,[4] a suggestion based upon experimental data was made, that the separation (S) of the central 10%, 20% and 30% isodose lines beneath a 70 cm. S.S.D. split field, with shield width d, was of the form:

$$S = 1.5d + \beta.$$

Values of β were tabulated for the 3 percentage isodose values, and for different depths below the skin surface, D. An analysis of further experimental data for 60 cm. and 80 cm. S.S.D., however, indicated that a more general relationship existed between penumbral isodose separation and size of lead shield, expressed in terms of the shadow d'', formed at depth D below skin surface.

The experimental arrangement is shown in Figure 1. A perforated dural tray was firmly attached to the head of the telecobalt unit and each lead shield was fixed to

* From the Department of Physics, The Royal Marsden Hospital, London, S.W.3, England.

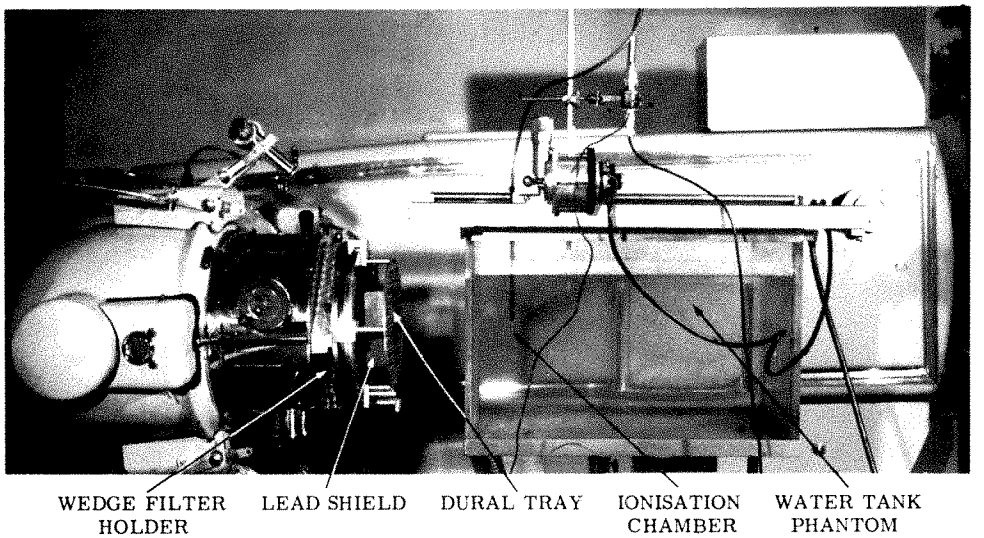


Fig. 1. Experimental arrangement for the measurement of a split field dose distribution.

the tray by clamping screws passed through three-quarter inch holes and screwed into the 3 mm. thick brass base-plate of the shield. The total height of each shield was 5.5 cm. A PTW micro-ionization chamber, measuring volume 0.05 cm.^{3}, whose movement in a water tank phantom was remotely controlled by a plotting device, enabled the dose to be measured at known points within the phantom. The shields were centrally placed within each field, and the penumbral regions at different depths D below the surface of the phantom were scanned. The positions of the 10%, 20% and 30% isodose values were recorded. The accuracy of reproducing a dose point position is estimated to have been ± 0.05 cm. Over 2,000 dose points were recorded for a total of 90 split fields, the parameters being varied as shown in Table 1.

An analysis of the isodose separations obtained from these dose points showed that for constant S.S.D., constant shield width d, and constant depth D (excluding $D=20$ cm.), the isodose separation for 20% and 30% could be regarded as independent of field size for clinical treatment planning purposes. The linear relationship $S=(\alpha \cdot d)+\beta$, although adequate if data for only a single value of the S.S.D. are required, does not lend itself to a more general application, since different values of α are required for each S.S.D., with a corresponding series of β values, and the calculations then become tedious. If, however, the equation is modified to $S=(\alpha'' \cdot d'')+\beta''$, where d'' is

Table I

SPLIT FIELD PARAMETERS

Parameter	Total No. of Values	Individual Values
S.S.D. (cm.)	3	60; 70; 80
Field Size (cm.)*	3 For each S.S.D.	23×12; 19×8; 15×6
Shield Width d (cm.)	10	1.77; 2.00; 2.42; 2.75; 3.18; 3.42; 3.94; 4.25; 4.59; 5.01
Depth below Surface D (cm.)	4	2; 8; 12; 20

* Individual values of the field sizes are stated at 70 cm. S.S.D. for 3 given positions of the diaphragm system.

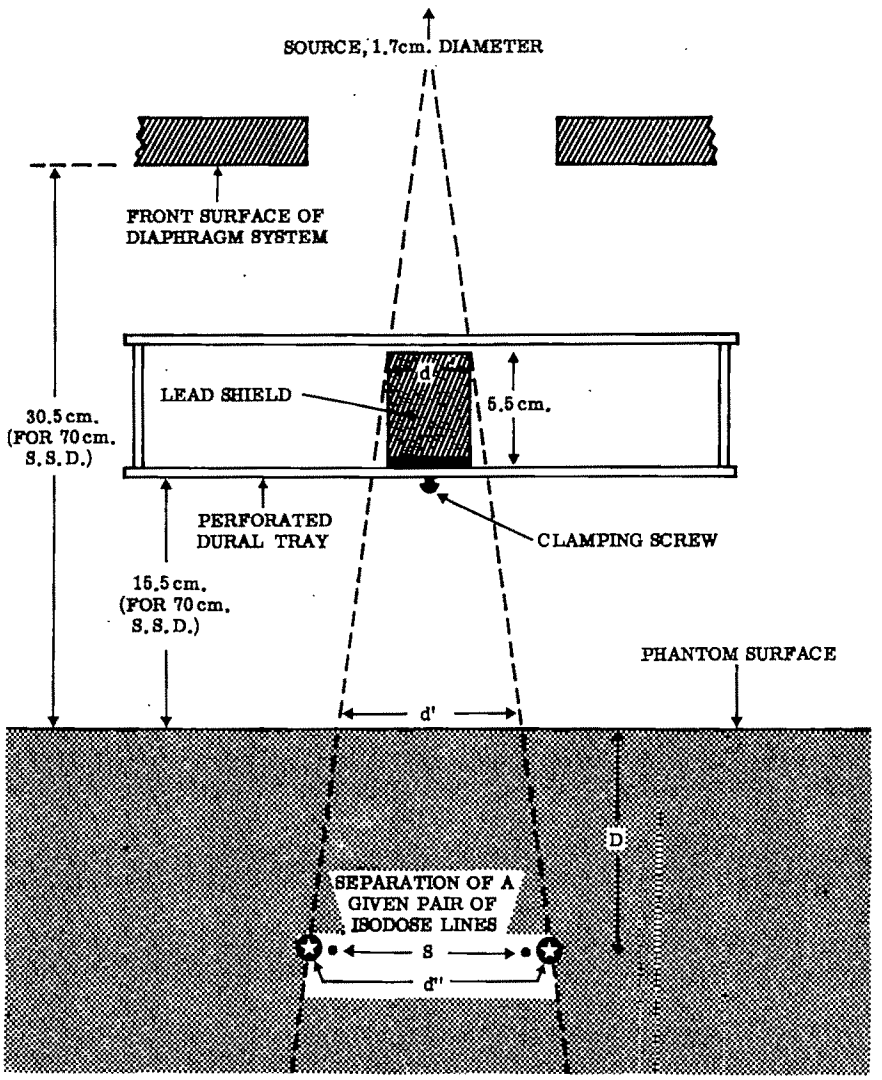


FIG. 2. The split field.

the shadow formed by the shield at depth D (Fig. 2), the value of α'' is independent of S.S.D.: see Table II, in which the values of α'' were calculated by the method of least squares using the University of London ATLAS computer.

A correction was applied to the computer calculated value of β'' to allow for small deviations in α'' from 0.98, and since β'' is a function of S.S.D., isodose value and depth D, it was found that the isodose separation S, which is independent of field size, could be expressed in the following way:

$$S = [0.98 \cdot d''] + [\gamma \cdot \text{S.S.D.}] + [\delta \cdot D] + \epsilon$$

Per cent Isodose	γ	δ	ϵ
20%	−0.02	0.025	0.70
30%	−0.01	0.025	0.30

The shield thickness of 5.2 cm. lead +0.3 cm. brass will allow a penetration of 2–3% of the primary radiation. The remainder of the radiation dose beneath the center of the shielded area, (ii), is due to scattered radiation. The variation of dose just below the surface of the shielded area consists of an initial decrease, or dose build-down,[3] which reaches a minimum value at 5 mm. to 7 mm. depth. Figure 3 illustrates this variation for a 15×15 cm. field at S.S.D.s 60

TABLE II

CALCULATED VALUES OF α'' FOR 1.77 cm. $\leq d \leq$ 5.01 cm.

Per Cent Isodose	Depth D (cm.)	S.S.D. 60 cm.	S.S.D. 70 cm.	S.S.D. 80 cm.
10*	2	0.96	1.02	1.02
20	2	0.96	0.97	0.96
20	8	0.99	0.98	0.98
20	12	0.99	0.98	0.98
30	2	0.96	0.97	0.96
30	8	1.00	0.98	0.97
30	12	1.00	0.98	0.98
Mean α''		0.98	0.98	0.98

* 3.18 cm. $\leq d \leq$ 5.01 cm.

cm., 70 cm., and 80 cm., with a 5 cm. shadow width d' on the skin surface. The maximum skin dose, measured at 0.075 cm. depth, is 21% for 60 cm., 15% for 70 cm., and 12% for 80 cm. S.S.D.s for the parameters of the telecobalt unit indicated in Figure 2. At depths greater than shown in Figure 3, the depth dose does not increase to more than 2–3% above the minimum dose value.

The depth doses along the central axes of the field portions adjacent to the shielded area, (iii), may be estimated from single

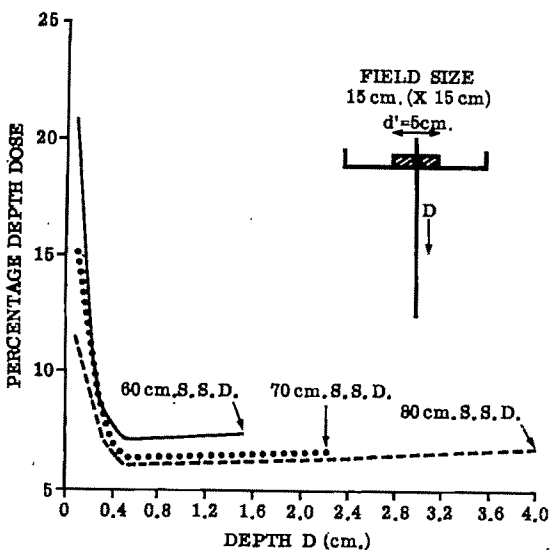


FIG. 3. Dose variation beneath the central shield.

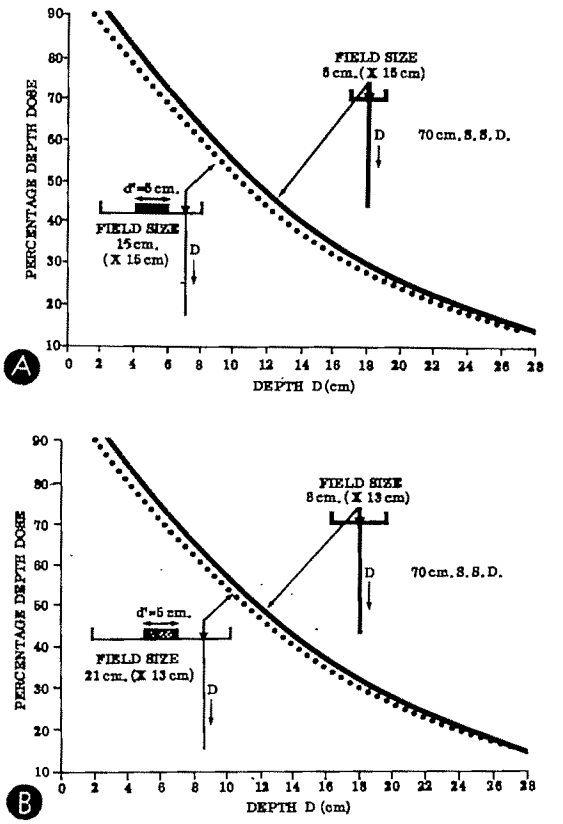


FIG. 4. (*A* and *B*) Split field depth doses.

field isodose curves of the same size. Figure 4, *A* and *B* illustrates the measured depth doses for two 70 cm. S.S.D. split fields with $d' = 5$ cm. and field sizes 15 cm. × 15 cm. and 21 cm. × 13 cm. In both cases, the split field depth dose is smaller than that measured for the 2 open fields 5 cm. × 15 cm. and 8 cm. × 13 cm. For the larger field, the error in assuming that the split field dose variation is the same as that of the open field is 3% of the local dose, and for the smaller field the error is 6% of the local dose. If a correction is applied to the central axis depth dose of the open field of similar size, amounting to 3%, 4%, 5% and 6% respectively, for 70 cm. S.S.D. field widths 8 cm., 7 cm., 6 cm. and 5 cm. respectively, the split field depth dose may be estimated. Finally, it is noted that the split field isodose curves in the regions adjacent to the central shielded zone are tilted slightly.[7]

SUMMARY

A formula has been derived from experimental data for 60 cm., 70 cm. and 80 cm. S.S.D. fields which enables the 20% and 30% central penumbral split field isodose separations to be calculated.

$$S = [0.98 \cdot d''] + [\gamma \cdot \text{S.S.D.}] + [\delta \cdot D] + \epsilon,$$

where d'' is the shadow of the shield at the depth of interest D, below the phantom surface, and γ, δ, and ϵ are functions of percentage isodose value. The variation of dose beneath the center of the shielded area is indicated. The relationship between the depth dose along the central axes of the field portions adjacent to the shielded area, and the central axis depth doses of open fields of the same shape is discussed.

Department of Physics
The Royal Marsden Hospital
Fulham Road
London, S.W. 3, England

I should like to thank Professor J. W. Boag and Dr. C. H. Jones of the Department of Physics, and Dr. M. Lederman of the Radiotherapy Department for their interest and encouragement. I am also indebted to Miss L. Pegus and Miss J. Scott-Elliot for the preparation and reproduction of the diagrams, and to Mrs. B. Wlodzik and the Radiography Staff for their willing co-operation.

REFERENCES

1. FLETCHER, G. H., MACCOMB, W. S., BALLANTYNE, A. J., SHALEK, R. J., and STOVALL, M. Radiation Therapy in the Management of Cancers of the Oral Cavity and Oropharynx. Charles C Thomas, Publisher, Springfield, Ill., 1962, p. 81.
2. FLETCHER, G. H. Textbook of Radiotherapy. Lea & Febiger, Philadelphia, 1966, p. 30.
3. JONES, C. H. Personal communication, 1967.
4. LEDERMAN, M., and MOULD, R. F. Radiation treatment of cancer of the pharynx. *Brit. J. Radiol*, 1968, *41*, 251–274.
5. PLANIOL, T., and DUTREIX, A. Dosimetric problems presented by protection of vital organs during transcutaneous radiotherapy. *Ann. radiol.*, 1962, *5*, 711–723.
6. SMITH, I. H., *et al.* Cobalt-60 Teletherapy: A Handbook for the Radiation Therapist and Physicist. Paul B. Hoeber, Inc., New York, 1964, p. 123.
7. WEBSTER, E. W., and TSIEN, K. C. Atlas of Radiation Dose Distributions. I.A.E.A., Vienna, 1965, p. 23 and Charts 84, 85, 86, and 87.

VOL. 105, NO. 1

PERMANENT INTERSTITIAL THERAPY USING LOW ENERGY AND LONG HALF-LIFE RADIATION SOURCES*

By JOSEPH E. SCALLON, M.D., CHARLES A. SONDHAUS, PH.D., SAMUEL L. SNYDER, M.D., BERNARD H. FEDER, M.D., *and* WALTER G. GUNN, M.D.
LOS ANGELES, CALIFORNIA

BIOLOGIC AND PHYSICAL BASIS

RECENT radiobiologic research has focused attention on the possibility of clinical application of protracted irradiation at low dose rate. The ability of cells to repair damage after a single radiation dose and the existence of a recovery threshold for low LET radiation has been demonstrated on populations of mammalian cells in culture.[1,2] Tissue radiation response is more complex than that of single cells but models have been devised to account for the effect of changes in dose rate, allowing the therapist to calculate the total dose of continuous irradiation over a given time equivalent to a single high dose rate exposure.[3,6] The partial recovery of latent injury in cells irradiated with small doses occurs in both tumors and normal tissues, and depends upon many factors including radiation quality, intracellular oxygen tension, size of dose, and other physical and biologic factors. The time-intensity factor was first expressed quantitatively by Strandqvist in 1944,[8] and the enhancement of radiosensitivity with oxygen in radiotherapy by Gray in 1961.[4] Given that a fraction of the cells in a tumor is anoxic, any means of increasing the relative radiosensitivity of this fraction can be expected to be important in radiotherapy. Among such methods are the use of heavily ionizing radiation, hyperbaric oxygen, and dose protraction. Recently, the last-named technique has begun to be considered more extensively; its efficacy depends on any differences in radiation response which may exist between tumor cells and normal tissue. Cellular differences, differences in tissue vascularity, and other complex biologic factors make it difficult, of course, to predict clinical response in terms of experimental results on simple systems.

Continuous low dose rate irradiation is clearly difficult externally, but interstitial implants appear to offer a means of continuous irradiation, if the level of background radiation emanating from the implanted patient can be reduced. The ease of shielding and the moderately long half-life of I^{125} suggested this isotope[5] as a means of solving the problem. Its low energy results in a negligible dose to the personnel performing an implant, and patient care is almost completely free from the necessity of elaborate requirements for radiation shielding and other personnel protection measures. On the other hand, within an implant itself, the distribution and uniformity of dose are comparable to that from a conventional implant of high energy emitter, *e.g.*, radon. The physical characteristics of the isotope, its incorporation into seeds designed for interstitial use, and the methods and results of *in vivo* dosimetry are briefly summarized here.

I^{125} is produced by neutron bombardment of Xe^{124}; it decays by electron capture to Te^{125} with a half-life of 60.2 days, emitting the fluorescent x-radiation characteristic of tellurium. The chief contributor to the dose is the K-alpha line, with energy 27.4 kev. The gamma ray dose rate constant for the isotope has been calculated as 1.23 r-hr.$^{-1}$

* Presented at the Sixty-eighth Annual Meeting of the American Roentgen Ray Society, Washington, D.C., September 26–29, 1967.
From the Departments of Radiology, the University of California; California College of Medicine, Los Angeles; South Bay Hospital, Redondo Beach; Los Angeles County General Hospital, Unit II; and Orange County Medical Center, Orange, California.
This investigation was supported in part by a research grant from the Attending Staff Association, Unit II, Los Angeles County General Hospital.

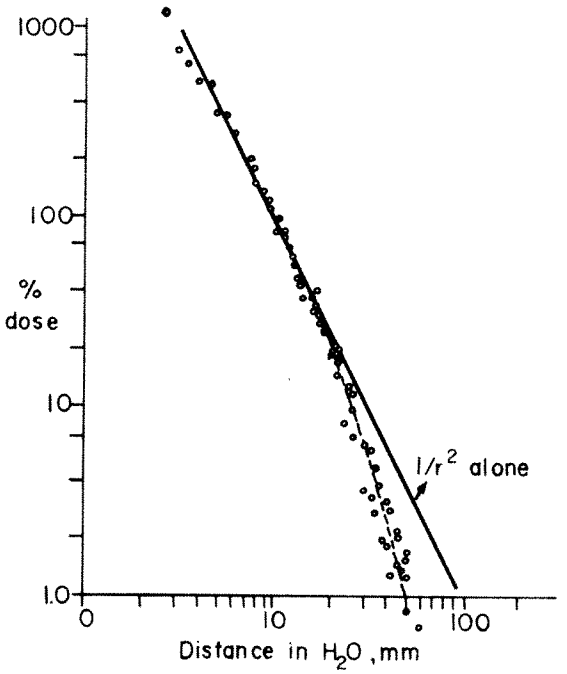


FIG. 1. Per cent of 1 cm. dose *vs.* distance in H_2O for I^{125}. Circles = experimental points. Solid line = inverse square law decrease alone.

per mc at 1 cm. Using the total energy absorption coefficient for this energy, the calculated half-value layer in water is 1.8 cm. This indicates that the dose distribution resulting from a 1 cm. spaced array of I^{125} sources should not differ appreciably from that of a standard Rn^{222} seed implant when due allowance is made for the difference in dose rate per unit source strength. The dose distribution around I^{125} sources, both singly (Fig. 1) and in arrays (Fig. 2), was accordingly investigated in both water and paraffin, and the half-value layer was measured in water (Fig. 3). In addition, the half-value layer was measured for both Ag and Pb shields.

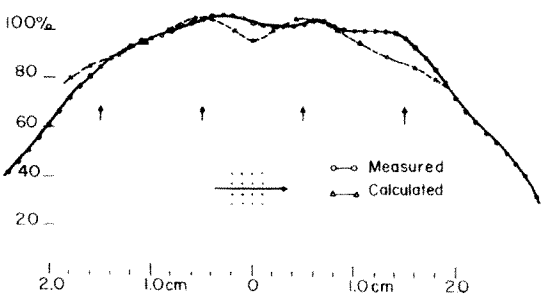


FIG. 2. Dose profile across center of 16 seed I^{125} implant in paraffin block, as per cent of central dose. Circles = measured values; triangles = calculated values.

I^{125} seeds were designed and developed in collaboration with the radiochemical group at the Hazleton-Nuclear Science Corporation, Palo Alto, California.* The design finally adopted consists of a plastic core containing an ion-exchange resin in which the isotope is bound; the core, in turn, is encapsulated in a titanium tube approximately 5 mils thick with welded closure at each end. The resulting source is 0.5 mm. in diameter and 4.0 mm. in length.

All sources were assayed individually by the manufacturer and grouped for delivery in terms of millicurie-equivalent source strengths; *e.g.*, the range 1.20–1.29 mc-equivalent indicated a source strength range which produced, in air, dose rates at 1 cm.-equivalent to unshielded sources with

* Now a branch of Isotopes, Inc.

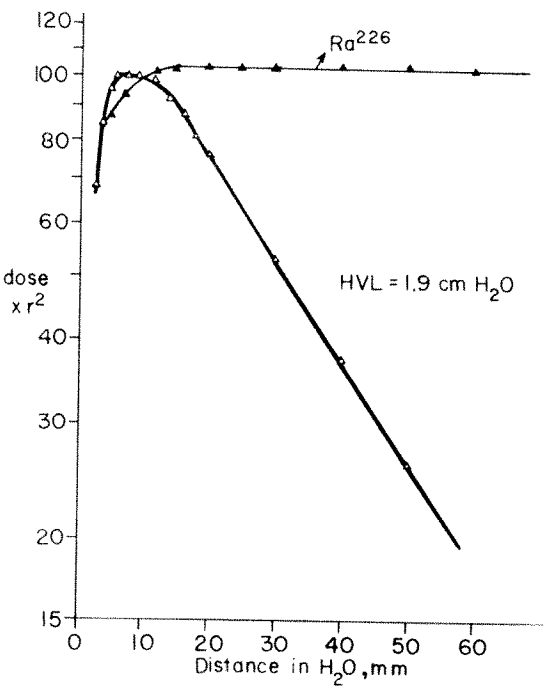


FIG. 3. Method of calculating half-value layer in H_2O for I^{125}. (Ra^{226} shown for comparison.)

this range of actual activities. Upon receipt of a source shipment, an approximate check of source strengths was made by reading the dose rate at a standard (20 cm.) distance using a Victoreen 440 ion chamber-vibrating reed electrometer survey instrument.

Dose measurements were made in both phantoms and tissue by the method of thermoluminescence dosimetry (TLD) using LiF phosphor[7] both as powder in teflon capsules and in the form of teflon rods 2.0 ×5.0 mm. in length, each containing 1.0 mg. of phosphor.* Figure 4 shows a seed and dosimeter; their sizes are indicated in centimeters. In using LiF as powder, each capsule was loaded with approximately 8–10 mg. of phosphor; catheter tubing was used and each end was plugged with small pieces of rod stock. All powder samples were weighed just prior to readout and the readings were expressed as counts per mg.; the corresponding doses were obtained by means of a calibration curve made for the same annealing run, using x-ray exposures at the same effective energy (100 kvp., half-value layer 2.6 mm. Al) and a low energy calibrated Victoreen thimble chamber. The LiF-teflon rods used were selected by exposing a group of rods to a fixed dose and choosing those rods for *in vivo* use which read identically to within ±5 per cent; about 60–70 per cent of a rod shipment met this specification. All readouts were made using a Con-Rad instrument.

For personnel monitoring, both photographic film and LiF as powder and teflon disks were used. TLD procedures were essentially the same as outlined above. Usually, one dosimeter was attached to the therapist's and physicist's right index fingers and another to their wrists; in addition, measurements were made on the face. Chest and abdominal dose monitoring was carried out on all personnel present during a procedure. Patient background dose rates were monitored after implantation by both TLD and survey meter measurements. Table I shows typical values of personnel exposure, while Table II gives average background dose rates in the vi-

* Controls for Radiation, Cambridge, Mass.; now a branch of Isotopes, Inc.

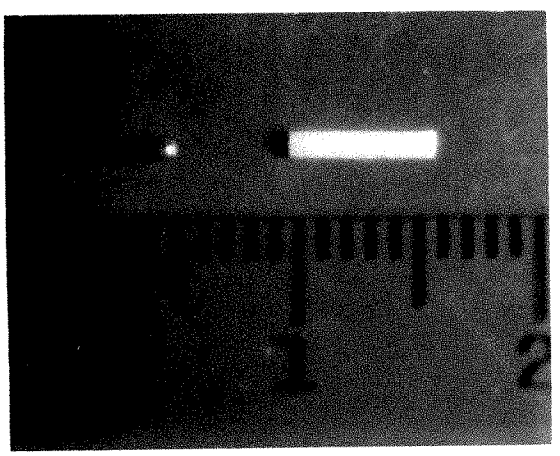


Fig. 4. I^{125} seed (left) and teflon rod-LiF dosimeter (right). Numerals on comparison scale = cm.

Table I

PERSONNEL EXPOSURE AT SURGERY

Case No.	No. of Seeds Implanted	Total Dose (mc-equivalent)	Average Dose to Hands (milliroentgen)	Average Dose to Trunk (milliroentgen)
1	27	29	5–10	5
2	20	14	15–20	5
3	18	13	5–15	5–10
4	22	24	5–20	5
5	9	8	5	5
6	7	7	5	5
7	17	4	5–25	5–15
8	9	11	5–10	5

Table II

AVERAGE PATIENT BACKGROUND DOSE RATES AT 18 INCHES (FRONTAL AND LATERAL)

Time Postoperative	Range of Dose Rates (milliroentgen/hour)
Immediate	0.5–3
2 weeks	0.5–3
1 month	0.3–2.5
2 months	0.2–2.0
4 months	0.2–0.8

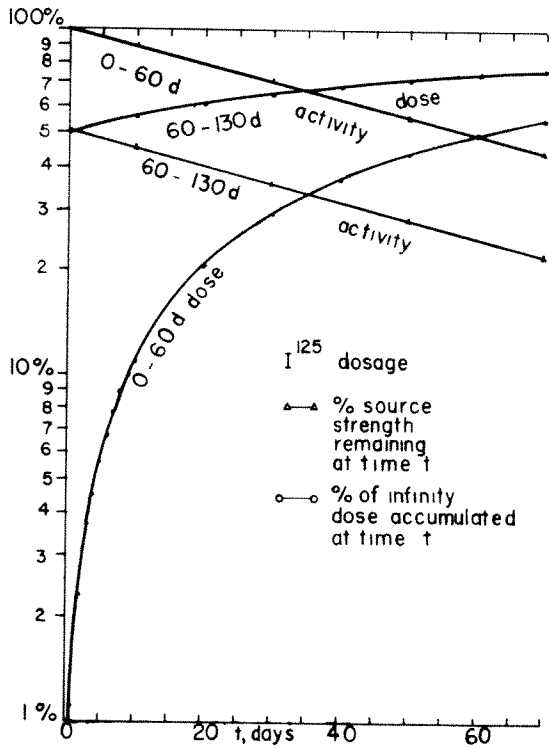


FIG. 5. Cumulative dose (circles) and dose rate (triangles) at time t for I^{125}; as per cent of infinity dose and per cent of initial dose rate.

cinity of the patient at several times after implantation.

From the results of dose distribution measurements on seed arrays in phantoms and their good agreement with calculated doses at selected points 0.5 cm. from the plane of the arrays, source strengths and spacings could be chosen beforehand in treatment planning. Source spacings used were 0.7, 1.0, or 1.4 cm., while source strengths ranged from 0.5 to 1.2 mc-equivalent among different implants. *In vivo* dosimetry was then performed on each implant to confirm the calculations. During the procedure, 2–4 teflon TLD rods were sutured in place at the surface of the implanted area, approximately 0.5 cm. from the plane of the seeds (Fig. 7*A*). Twenty-four to 48 hours later, the rods were removed and read; total dose at that point in the implant at any time thereafter was then estimated by use of the graph shown in Figure 5. The curve depicts dose rate as per cent of initial value and total cumulative dose as per cent of infinity dose at any time for the I^{125} half-life of 60.2 days. If, for example, a total dose of 230 rads was received by a rod in 2 days, at which time 2.3 per cent of the infinity dose had been delivered, it can be seen that the dose at infinity will be 10,000 rads at that position, and that the dose at 60 days (one half-life) will be 50 per cent of that value, or 5,000 rads.

The dose within a plane 0.5 cm. from the implant plane was calculated to be uniform within ± 10 per cent out to 0.5 cm. beyond the perimeter of a 16 seed, 1.0 cm. rectangular spaced array, and phantom measurements confirmed this approximate rule.

CASE SELECTION AND METHODS OF STUDY

Only epidermoid carcinomas of the head and neck were selected for this study. It was thought that close observation of tissue reaction could be made in this location. In all, 8 patients were included. These cases consisted of a recurrent carcinoma of the left orbit following enucleation; two lesions of the tonsil; two epidermoid carcinomas of the anterior two thirds of the tongue; and three similar lesions involving the soft palate. Five cases had undifferentiated types of tumor; three were of intermediate grade, and only one was a well differentiated epidermoid carcinoma of the tonsil. All cases were considered rather far advanced with involved cervical lymph nodes.

With the exception of one case, all patients had received prior external irradiation using cobalt 60 teletherapy or from a 4 mev. linear accelerator. The one exception was of a recurrent carcinoma of the soft palate which had received cobalt 60 teletherapy and had recurred within 6 months. The tumor dose in preoperative irradiation ranged from 2,000 to 6,500 r, over 2 to 8 weeks time. Interstitial implantation was performed 1 to 4 weeks after the completion of external radiation therapy.

The dose from the interstitial irradiation varied in each case depending on the previ-

ous external therapy plus the size and location of the primary lesion. In general, the dose was calculated to correspond to 4,000–5,000 r using radium (1,000 r/day). The dose equivalent for I^{125} was arrived at by extrapolation from Strandqvist's curve and by an RBE correction for the energy difference between radium and I^{125}. The final correction factor was estimated as a 20 per cent dose increase compared to standard radium or radon dosages. It was believed by the authors that this was probably a low estimate. The effects of the decay factor, long half-life, and low energy of I^{125}, of course, represent some of the major uncertainties in permanent implants made with this isotope.

All of the implantations were performed in the surgical suite under general anesthesia. The technique of implantation was similar to that used with radon seeds. The area to be implanted was carefully measured and the site of each seed to be implanted was carefully delineated by marking with a Bovie Cautery. Standard radium needle inserters were used and we attempted to place the seeds approximately 1.0 cm. apart* and 0.5 cm. beneath the surface of the mucosa or skin. With the use of straight needle inserters, a significant seed loss was noted during the first 2 months of follow-up. Thereafter, we changed to curved needle inserters in an effort to bury the seed as far as possible from the point of insertion. This produced an improvement in seed retention at the implanted site.

The lithium fluoride dosimeters were fixed in place by first tying a loop of 3–0 silk suture around the rod and then stick-tying this into the mucosa (Fig. 7*A*). These dosimeters were removed easily by merely tugging forcefully on the suture after the second to the fourth day. No bleeding was encountered after removal of the dosim eters.

For protection, fluoroscopic lead aprons were worn. Table 1 shows the relatively low doses received by the radiologist. It must be noted that the dose to the trunk represents measurements made in front of the lead apron and that actual exposure to the trunk (behind the lead apron) was too low to be measured with our equipment.

The patients were usually discharged from the hospital 1 to 2 days after implantation. Postoperative roentgenography was performed the following day to check on seed placement, and then every 2 weeks to 1 month thereafter. Monitoring of the patient was done using the Victoreen 440 ion chamber-electrometer survey instrument. Readings were taken at 18 inches directly in front of the patient and at 18 inches laterally. Determinations were made at standard intervals postoperatively. Table 11 shows the dose rates obtained.

OBSERVED CLINICAL REACTIONS AND CONCLUSIONS TO DATE

None of the patients experienced any severe discomfort during the immediate postoperative period. There was no occurrence of bleeding or marked mucosal edema. On postoperative roentgenograms (Fig. 6, *B* and *C*) the seeds were more difficult to identify than radon or gold seeds due to the low Z number of the titanium. Because of this, a small gold sphere was placed in the middle of each seed thereby helping in its identification.

The reactions observed to date appear to be quite different, depending upon the area of implantation. In the first case, where the skin over the left orbit was implanted, the initial skin reaction was seen in approximately 4 weeks and gradually healed in 3 months. There was no wet desquamation—rather, a dry denudation of the overlying skin and again, gradual repair (Fig. 6, *D* and *E*).

A much different reaction has been noted in those cases involving the soft and hard palate. Here, the initial reaction was a slight grayish discoloration of the mucosa accompanied by minimal edema. This occurred in approximately 2 weeks. In 6 weeks to 2 months, punctate yellowish granular necrosis began immediately above

* 0.7 cm. and 1.4 cm. in 2 cases.

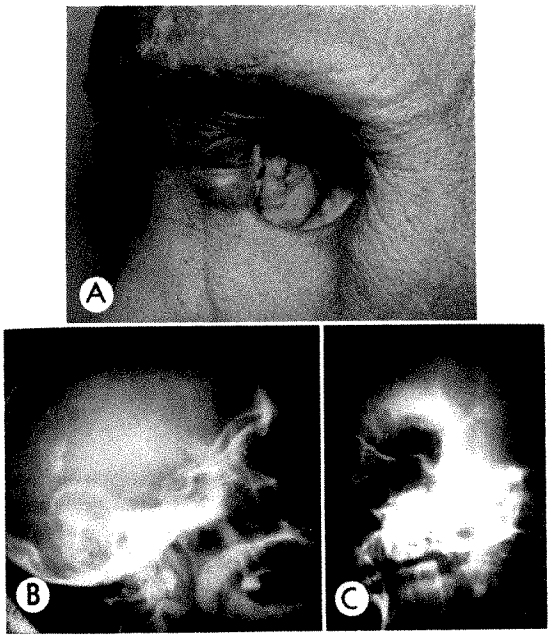


FIG. 6. Case 1. A 55 year old Negro male with epidermoid carcinoma originating in the left maxillary antrum and extending to the ethmoids and medial aspect of the left orbit. Left antrectomy, ethmoidectomy, and left orbital exenteration in October, 1965 were followed by postoperative irradiation with 5,000 r tumor dose to the entire area. (*A*) *Recurrence*, July 1966, along medial aspect of the left orbit extending medially to the skin margin. (*B* and *C*) Lateral and oblique roentgenograms showing I^{125} seed placement; the rounded metallic densities are small gold spheres each located in the center of an I^{125} seed.

the site of each seed (Fig. 7*B*; and 8*B*). This gradually increased and became confluent in 3 to 4 months (Fig. 7*C*; and 8*C*). Minimal slough of the necrotic tissue occurred during this time but became more obvious in the sixth and seventh months (Fig. 7*D*; and 8*D*). There did not appear to be any significant reparative process and in fact, in one case, there was seen gradual destruction of the entire soft palate and in another case a painless, slow destruction of the hard palate. In these same patients the granular necrotic reaction was seen in the region of the hypopharynx (which was also implanted) although at the time of this publication, it appears to be subsiding and a reparative process is taking place.

This granular reaction does not appear to be a normal mucositis as is seen during the use of radon or radium. Instead, the tissue has the appearance of "paté" which can easily be removed with a cotton swab. No bleeding has accompanied this.

The patients have had mild to moderate discomfort usually occurring in approximately 2 months and subsiding in 5 to 6 months. This would coincide with the period of noticeable tissue destruction.

In summary, we have implanted 8 pri-

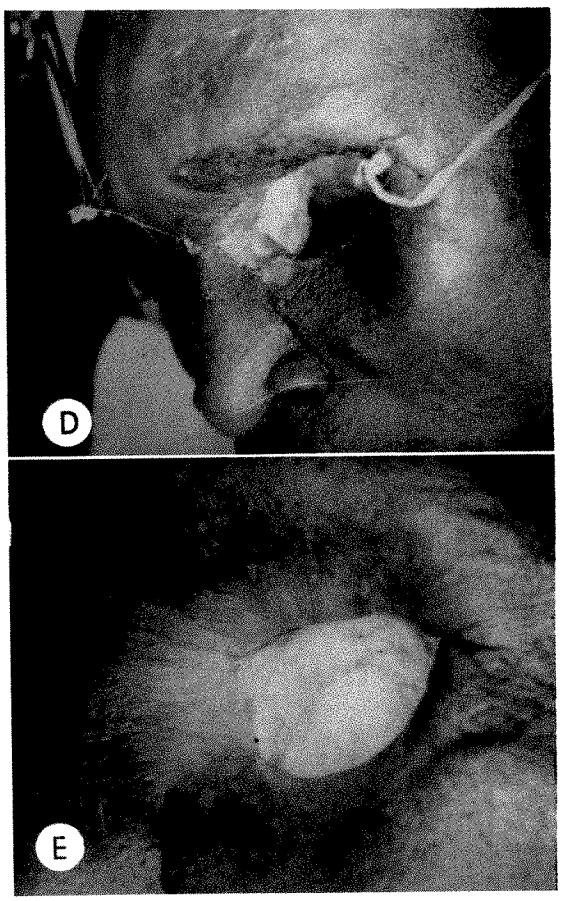


FIG. 6. (*D*) *One month after implantation.* There is marked regression of tumor in the medial aspect of the left orbit with denudation of epithelium. Stay sutures had been used to hold packing in place within the orbit for 3 weeks postoperatively. (*E*) *Three months after implantation.* Complete healing of the implanted skin has taken place. Marked fibrosis is present within the orbit with no visible residual tumor. Note end of one seed protruding from the surface.

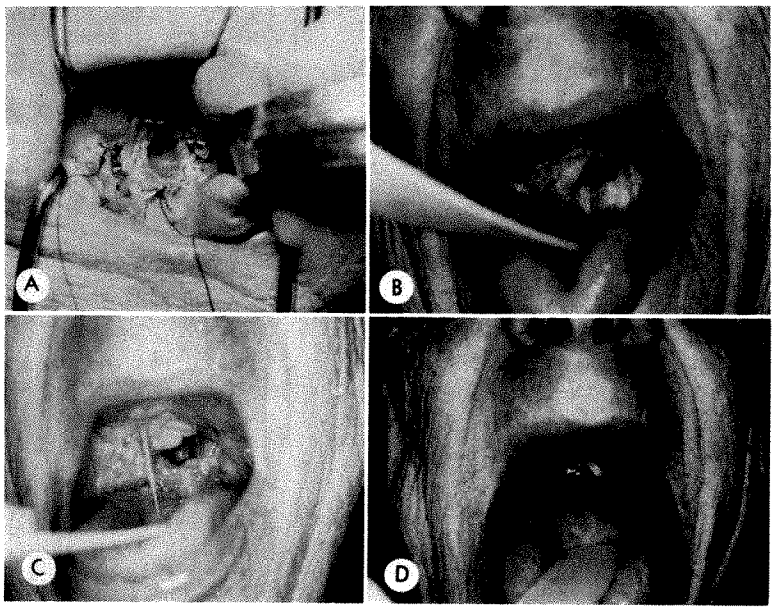


FIG. 7. Case III. This 65 year old white female with advanced squamous cell carcinoma of the soft palate extending down the glossopalatine folds was given 6,500 r tumor dose in 7 weeks using cobalt 60 teletherapy. Despite marked regression of the tumor, residual carcinoma was believed to be present on subsequent follow-up examinations. Implantation of I^{125} seeds was performed 7 weeks following completion of external radiation therapy. (*A*) Photograph taken at surgery, immediately following implantation of 18 I^{125} seeds into the posterior aspect of the hard palate, soft palate, and palatopharyngeal folds; 4 lithium fluoride dosimeters are tied to the mucosa. Note hole in the soft palate from neoplastic erosion. (*B*) *Two months after implantation.* Slight edema and grayish reaction is still present along the posterior border of the soft palate. Granular, yellow, necrotic reaction is now beginning to appear in the right side of the soft palate. (*C*) *Four months after implantation.* The granular necrotic reaction has reached its maximum extent and is now present over the anterior and right lateral sides of the palate. This reaction now extends into the lateral hypopharynx. (*D*) *Six months after implantation.* Slough has occurred with loss of a major portion of the soft palate; no visible tumor is present.

mary epidermoid carcinomas of the head and neck using I^{125} seeds. Although it is too early for complete evaluation, it would appear that the area implanted has much to do with the expected reaction. In implantation of the tongue, there appears to be an onset of confluent mucositis; quite soon thereafter, a slow, reparative phase taking many months. A similar response is seen in implantation of areas of skin with denudation occurring in 1 month with complete healing seen in approximately 2 to 3 months.

The reaction over the soft and hard palate appeared to show a greater degree of slow mucosal destruction with associated sloughing and no marked reparative process. The authors feel that decrease in vascular supply due to constant irradiation over a long period of time may play an important role.

SUMMARY

Eight patients with head and neck carcinoma were treated using permanent interstitial implants of radioactive I^{125} seeds. A marked decrease in radiation exposure to the medical personnel was achieved. The monitoring of the patients following surgery revealed that they emitted acceptably low levels of radiation for their out-patient status. Reactions to date differ depending upon the area implanted, although all show a slow buildup of maximum reaction. There is a paucity of reparative process seen in those cases where the palate was im-

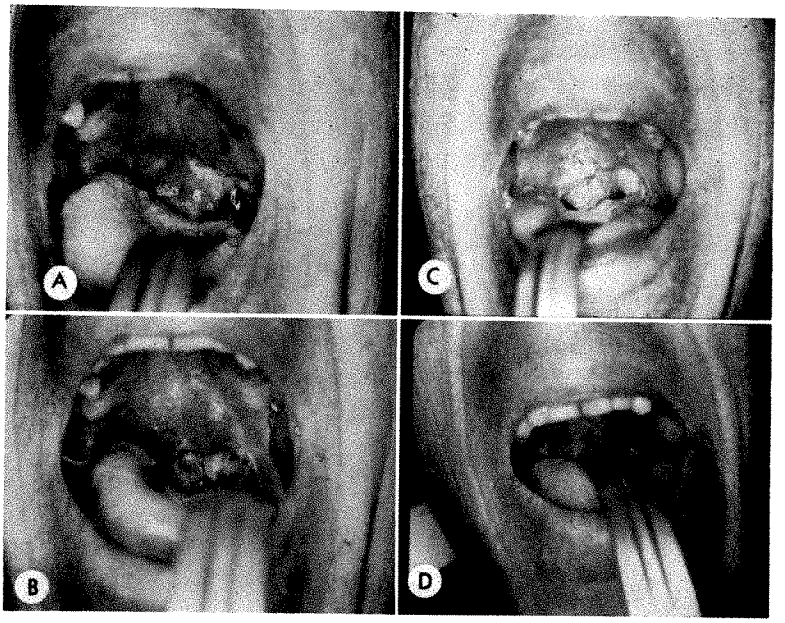


FIG. 8. Case v. This 57 year old white male with an ulcerating anaplastic epidermoid carcinoma of the soft palate was given 5,100 r tumor dose using cobalt 60 teletherapy with only a minimal decrease in tumor size observed during treatment. Immediately following completion of external irradiation, the area was implanted with 10 I^{125} seeds. (*A*) *Four weeks after implantation.* The ulcerative lesion is still visible in the left soft palate; no granular necrotic reaction has yet appeared. (*B*) *Two months after implantation.* Minimal necrotic reaction is beginning to appear in the center and along the right lateral aspect of the implant; the actual ulceration now appears to be enlarging. (*C*) *Three and one-half months after implantation.* Maximum granular necrosis ("paté") has now developed. (*D*) *Four months after implantation.* Slough of the necrotic area has occurred. The patient continues to have marked pain in this region.

planted. Close follow-up of these patients will be continued and, if possible, microscopic sections of the implanted tissue will be obtained.

Joseph E. Scallon, M.D.
South Bay Hospital
514 North Prospect
Redondo Beach, California 90277

The authors wish to express their gratitude to Dr. G. D'Ablaing (Pathologist; Los Angeles County Hospital, Unit II) for his generous advice and assistance in preparation of the specimens and to Mrs. Marilyn Hartnell for her help in preparing the manuscript.

REFERENCES

1. BERRY, R. J., and ANDREWS, J. R. Quantitative relationships between radiation dose and reproductive capacity of tumor cells in mammalian system *in vivo*. *Radiology*, 1961, *77*, 824–830.
2. ELKIND, M. M. Cellular aspects of tumor therapy. *Radiology*, 1960, *74*, 529–541.
3. FOWLER, J. F., and STERN, B. E. Dose-rate effects: some theoretical and practical considerations. *Brit. J. Radiol.*, 1960, *33*, 389–395.
4. GRAY, L. H. Radiobiologic basis of oxygen as modifying factor in radiation therapy. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1961, *85*, 803–815.
5. HARPER, P. V., LATHROP, C. A., BALDWIN, L., ODA, Y., and KRYSHTAL, L. Isotopes decaying by electron capture: new modality in brachytherapy. *Isotopes in Med.*, 1958, *26*, 417–422.
6. LAJTHA, L. G., and OLIVER, R. Some radiobiological considerations in radiotherapy. *Brit. J. Radiol.*, 1961, *34*, 252–257.
7. Luminescence Dosimetry. Edited by F. H. Attix. USAEC-CONF-650637, April, 1967.
8. STRANDQVIST, M. Studien über die kumulative Wirkung der Röntgenstrahlen bei Fraktionierung. *Acta radiol.*, 1944, Suppl. 55.

Vol. 105, No. 1

CLINICAL APPLICATION OF COMPUTER DOSIMETRY IN INTERSTITIAL RADIUM THERAPY*

By JOSEPH R. CASTRO, M.D., ROBERT D. LINDBERG, M.D., *and* GILBERT H. FLETCHER, M.D.
HOUSTON, TEXAS

A BASIC program that produced, within limitations, dose distributions for interstitial radium needle implants[12] was initiated at the M. D. Anderson Hospital in the early 1960s. The detailed mathematical and physical bases for these programs have been described elsewhere[1,11,12,13] and thus are only briefly summarized. The original program was limited by the assumption that the needles either intersected the plane of calculation at right angles or were parallel to the plane of calculation. In addition, the format of input into the program was limited and the output was in the form of a grid from which hand-drawn isodose curves were constructed.

The present RADCOMP program eliminates the above restrictions. The radium sources are localized from either orthogonal or stereoscopic roentgenograms and assigned Cartesian coordinates for input into the program. Planes of calculation desired by the radiotherapist may be selected at any relationship to the needles. The needles need not intersect the plane or be at any special angle to the plane. An appropriate grid, usually 2 mm. in size, is centered on the desired plane of calculation. The dose at each point of the grid is calculated using the Sievert integral, summing the contribution from each radium source. The program generates the contribution from each source as it runs, rather than relying on stored tables. This allows for ready introduction into the system of new radium sources or different isotopes. Preselected isodose curves are drawn by a program plotting routine, thus making the output available in an easily understandable form. The versatility and usefulness of the program has been tested over a period of 2½ years.

The present experience, since 1961, consists of over 100 interstitial radium needle implants almost all for lesions of the anterior two-thirds of the tongue and floor of mouth. The purpose of this paper is to relate some of the problems encountered in translating the previous experience at the M. D. Anderson Hospital using Paterson-Parker stated dose calculations to the use of computer-obtained dose data.

PATERSON-PARKER STATED DOSE

In the Paterson-Parker system of dose specification for interstitial radium,[6,7] the stated dose for single plane implants is allegedly 10 per cent above the absolute minimum dose on a plane 0.5 cm. from the plane of the needles (Fig. 1). In double plane implants at a separation of 1.0 cm. the stated dose is given on a plane midway between the planes of the needles. In volume implants the stated dose is again 10 per cent above the absolute minimum dose within the implanted volume and dips 3 to 4 mm. within the physical shell of the needles at points between the needles. The stated dose obtained from the Paterson-Parker tables[5] is specified as having an accuracy of ±10 per cent when the distribution rules are followed. Dosage recommendations for interstitial implants are based on 7,000 gamma roentgens in 7 days (more recently 6,500 roentgens) with appropriate reductions for shorter times.[8,9] Paterson suggested that the optimal dose in larger volume implants is lower than for small implants.[8,9]

* Presented at the Fiftieth Annual Meeting of the American Radium Society, Miami Beach, Florida, April 7–11, 1968.
From the Department of Radiotherapy, The University of Texas M. D. Anderson Hospital and Tumor Institute at Houston, Houston, Texas.
This investigation was supported in part by U. S. Public Health Service Research Grants No. CA-06294 and CA-05654.

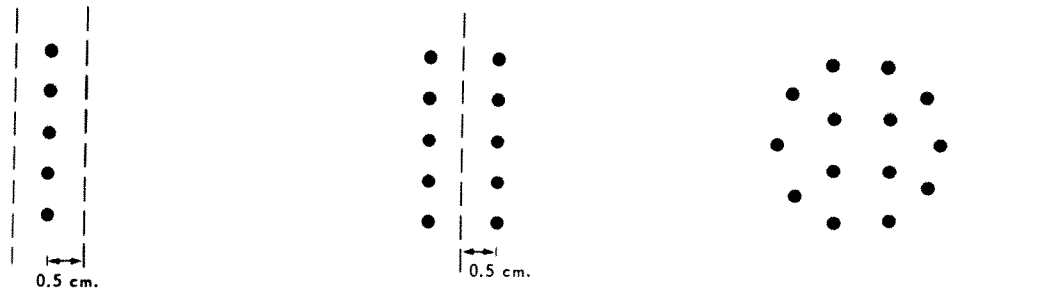


FIG. 1. Schematic diagram of the dose specification in the Paterson-Parker system. The stated dose is specified to a plus or minus 10 per cent accuracy and lies 10 per cent above the absolute minimum dose, except in the immediate vicinity of the needles. The stated dose is obtained from the tables.[5]

It has been determined by manual and computer calculations that using the Paterson-Parker distribution rules, the actual dose 0.5 cm. from the plane of the needles may be as much as 15 to 20 per cent lower than the stated dose[4,10] depending on the size of the implant. In contrast, using the same intensity needles throughout single plane implants, the dose actually delivered is only 5 to 15 per cent more than the stated dose, depending on the size of the implant.[4,10] For double plane implants, with a 1 cm. separation between the planes, the dose between the planes is greater than the dose 0.5 cm. lateral to each plane. A closer correlation of doses between the planes and 0.5 cm. lateral to the planes is obtained when 1.5 cm. separation is used.[10]

POLICIES PRIOR TO COMPUTER DOSIMETRY

Even prior to the advent of computer dosimetry and in view of these relationships, uniform intensity needles were used throughout the implant (0.66 or 0.33 mg./cm.). Deviations from the distribution rules were often required because of anatomy and extent of the disease. Calculated tumor doses of 7,500 to 8,000 gamma roentgens in 6 to 7 days, or 7,000 gamma roentgens in 4 to 5 days were often given in the treatment of anterior tongue lesions,[3] particularly if the lesion was infiltrative. Somewhat lower doses (5,500 to 6,000 gamma roentgens in 5 to 6 days) were used in lesions of the floor of the mouth. Large volume implants received the same or, in some cases, a higher dose than small implants, in contrast to Paterson's recommendation to decrease the dose 500 to 1,000 gamma roentgens for large volumes. In selected cases when external irradiation and radium implantation were combined, 7,000 roentgens in 4 weeks were given.

In 1961 a retrospective analysis[2] was made of intra-oral interstitial implants by obtaining computer dosimetry on those cases which showed either local recurrence or necrosis. Positive correlation was found between necrosis and high dosage areas caused by bunching of needles or high dose rate implants (6,000 roentgens given in 70 to 100 hours); similarly there was correlation between cold areas and recurrence.

POLICIES USING COMPUTER DOSIMETRY

PHASE I

Shortly after computer dosimetry became available (January 1961), the dose specification was converted from roentgens to rads.[10] Otherwise, the time-dose relation-

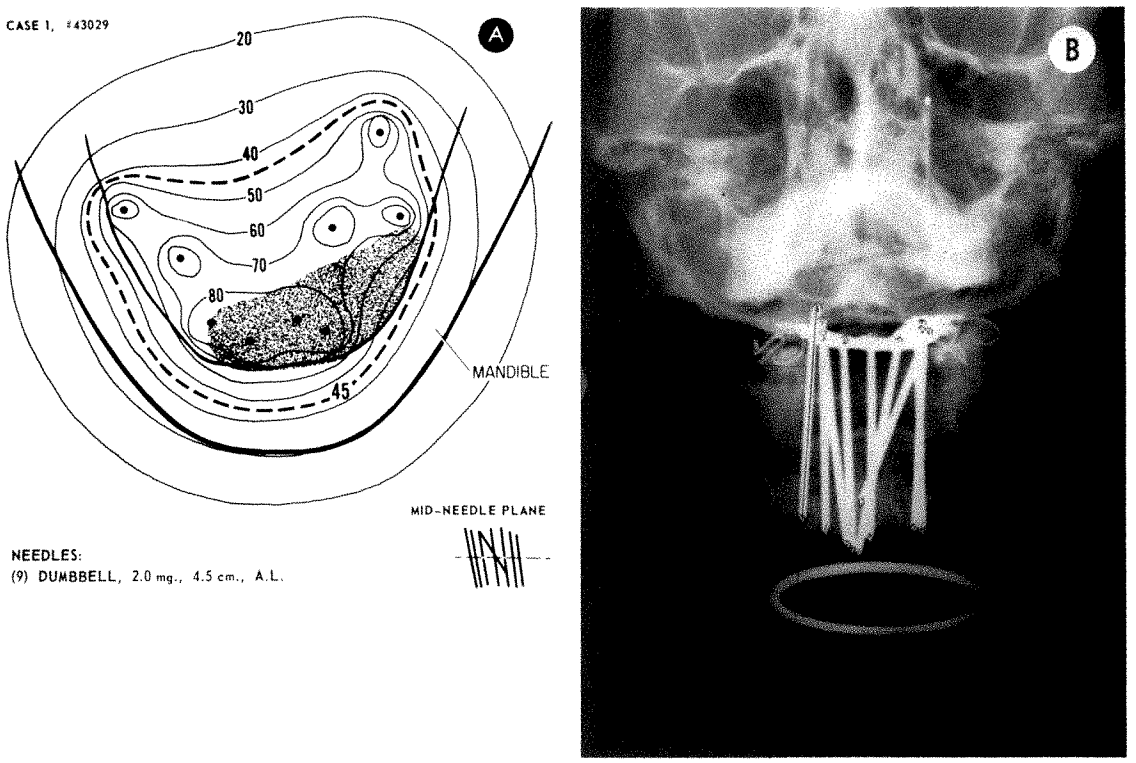


FIG. 2. (*A* and *B*) Plane of calculation perpendicular to the needles and transecting them at their midpoint. This is a hand-drawn isodose distribution from an earlier version of the computer program. Rerunning the case with the latest version and obtaining computer-drawn isodoses revealed essentially the same isodose distribution. The approximate tumor outline is shown. The selected 45 rads per hour isodose includes a generous tissue volume and a portion of the mandible, felt necessary because the tumor was adherent to the mandible.

ships in use prior to the onset of computer dosimetry were unchanged. Therefore, since the conversion factor is 90 rads = 100 roentgens, in effect the dose was increased 10 per cent. A partial biologic correction was made by using lower intensity needles, *i.e.*, 0.5 or 0.25 mg. per cm. rather than 0.66 or 0.33 mg. per cm. needles. A generous minimum tumor dose was selected from the computer isodoses, knowing that the computer minimum tumor dose could be as much as 20 per cent more than the stated dose as determined by Paterson-Parker tables.

During the latter half of 1961 and 1962, 30 intra-oral interstitial implantations were done. Table 1 shows a low recurrence rate during this period but a high incidence of complications, specifically soft tissue necrosis and osteoradionecrosis. The following case is an example of the problems encountered during the period:

CASE 1. This 66 year old white female was first seen in March, 1962 with a squamous cell carcinoma of the anterior floor of the mouth extending to the left of the midline, involving the lower gum, and attached to the periosteum of the mandible. The lesion also crossed to the right of midline and extended posteriorly in the left lower gingival sulcus. A small 1.5 cm. submental lymph node was palpable. The lesion was staged as a T_2N_1 lesion. A radium needle implantation was done using 4.5 cm. active length dumbbell needles (2 mg. radium each). Forty-five rads per hour isodose was chosen encompassing generously the lesion and a large portion of the mandible (Fig. 2, *A* and *B*). A dose of 5,830 rads was delivered in 120 hours. The previously palpable submental lymph node disappeared.

Three months postimplantation she de-

TABLE I

ORAL CAVITY LESIONS TREATED BY RADIUM NEEDLING
(Computer Dosimetry Available)

Time Periods	1961 and 1962*		1963 and 1964*		1965 and 1966†	
Sites	Anterior 2/3 of Tongue	Floor of Mouth	Anterior 2/3 of Tongue	Floor of Mouth	Anterior 2/3 of Tongue	Floor of Mouth
Soft tissue ulceration	15/20–75%	8/10–80%	15/28–54%	9/12–75%	14/21–67%	6/10–60%
Bone necrosis and surgery required on number of patients treated	2/20–10% 2/20	4/10–40% 2/10	5/28–18% 1/28	2/12–17% 1/12	5/21–24% 1/21	2/10–20% 1/10
Primary recurrence	3/20–15%	0/10–0%	9/28–32%	1/12–8%	1/21–4.8%	0/10–0%

* 2 year follow-up.
† Analysis, February 1968, minimum 15 month follow-up.

veloped a small area of exposed bone in the inner surface of the mandible. Despite treatment with zinc peroxide packs and irrigation, this continued to enlarge and became subsequently more painful. In October, 1962 a partial resection of the mandible and floor of the mouth was done with application of split thickness graft. No evidence of residual recurrent tumor was seen. Continued zinc peroxide packs and irrigations were used and by June, 1963, almost all areas of exposed bone had disappeared. She has continued to be followed closely with only occasionally minute sequestra. Since 1965 this has ceased completely and at present there is no evidence of osteoradionecrosis or tumor.

PHASE II

In January, 1963, because of the increased incidence of complications, the dosage was reduced by 10 per cent, a less generous minimum tumor dose was selected and the dosage rate lowered.

Under this time-dose scheme during the following 2 years (1963 and 1964) there was a decrease in complications, but the local recurrence rate increased in the tongue lesions, although not in the floor of the mouth (Table 1). An example of this type of recurrence is illustrated in the next case:

CASE II. This 55 year old white male presented with an ulcerative lesion of the left lateral border of the tongue measuring 3×1×2 cm. A central ulcerated area, 1.0×1.5 cm. was present. No cervical lymphadenopathy was noted and the lesion was staged as a T_2N_0 lesion. He was treated with a single plane radium needle implantation of the left lateral border of the tongue, utilizing 0.5 mg. per cm. needles (active length 4.5 cm.) in the palisade with a crossing needle of 0.66 mg. per cm. intensity. The implant delivered 7,000 rads in 200 hours.

Initially following treatment the patient did well, but 5 months later there was recurrent disease in the tongue together with a partially fixed left upper cervical lymph node. The lymph node received preoperative irradiation of 1,250 rads in a single dose, using the cesium 137 unit, following which a left hemiglossectomy and hemimandibulectomy with radical neck dissection were done. Recurrent disease was present in the tongue. He has since been followed for a period of 3 years and there is no evidence of recurrent disease or metastasis. The recurrence in this case was probably related to the relatively prolonged treatment time (200 hours) to deliver 7,000 rads (Fig. 3, *A* and *B*).

PHASE III

Because of the increased recurrence rate in tongue lesions, the treatment policy was again modified in January, 1965 by adding external irradiation prior to the radium implantation (except for the very early lesions) with time-dose factors which differ for the anterior two-thirds of the tongue and the floor of the mouth.[4]

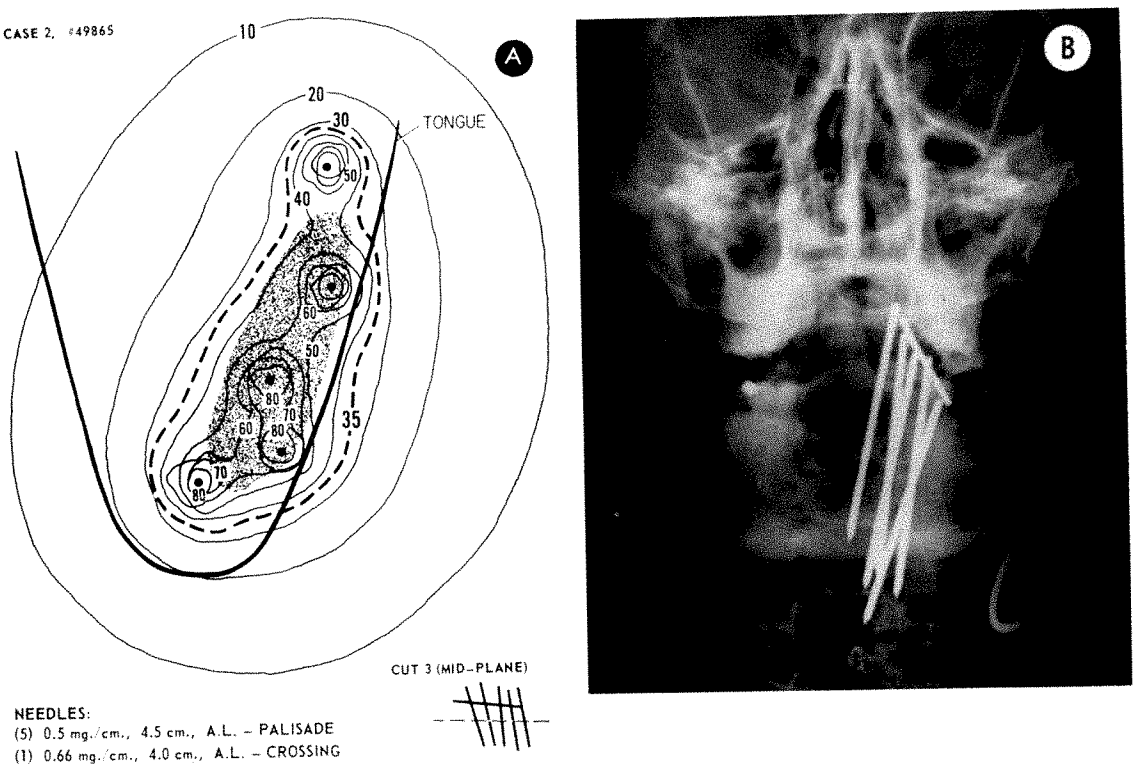


FIG. 3. (*A* and *B*) Plane of calculation at the midpoint of the needles. The lesion measured 1.0×3.0 cm. with an approximate depth of 2.0 cm. in the left lateral border of the tongue.

In early lesions that can be encompassed by a small or moderate size implant (T_1) 2,000 rads tumor dose is given with external irradiation in 5 to 6 treatments as a preneedling dose. In T_2 and T_3 lesions, 3,000 to 5,000 rads tumor dose in 3 to 5 weeks is given preneedling with external irradiation, particularly in lesions which because of location or size may produce a poor geometric implant.[4]

Every attempt is made to have the implant dose rate less than 40 rads per hour. Particularly in the floor of the mouth a less generous minimum tumor dose is selected than for the anterior two-thirds of the tongue because of the lesser radiation tolerance due to a thin mucous membrane over loose connective tissue and bone. Low intensity needles, 0.25 mg. per cm. or 0.33 mg. per cm., are used to keep the dose rate low. The following case illustrates the new policy:

CASE III. This 37 year old white male presented with an exophytic lesion of the anterior floor of the mouth measuring 1.5×3.0 cm. in size and crossing slightly to the left of midline. Initially no cervical lymph nodes were palpable. After teeth extraction the lesion received 4,000 rads tumor dose via a submental field in 23 days using the 18 mev. electron beam, followed by a volume implantation delivering 4,000 rads in 89 hours. The isodose of 45 rads per hour (Fig. 4, *A* and *B*) was selected despite areas of possible underdosage where the 45 rad per hour isodose curves are not joined. The 30 rads per hour isodose encompasses all of the implant, but selecting this isodose curve would have resulted in more than doubling the volume receiving the minimum tumor dose, *i.e.*, a small shift in isodose results in a deceptively large increase in treated tissue volume. Also the mandible would have received a much higher dose. Nine months postimplantation a 0.2 ×0.5 cm. area of exposed bone appeared but healed eventually with conservative therapy (zinc peroxide packs and irrigation). If one had selected 30 rads per hour isodose, the bone exposure would have been more severe with possible mandibular necrosis.

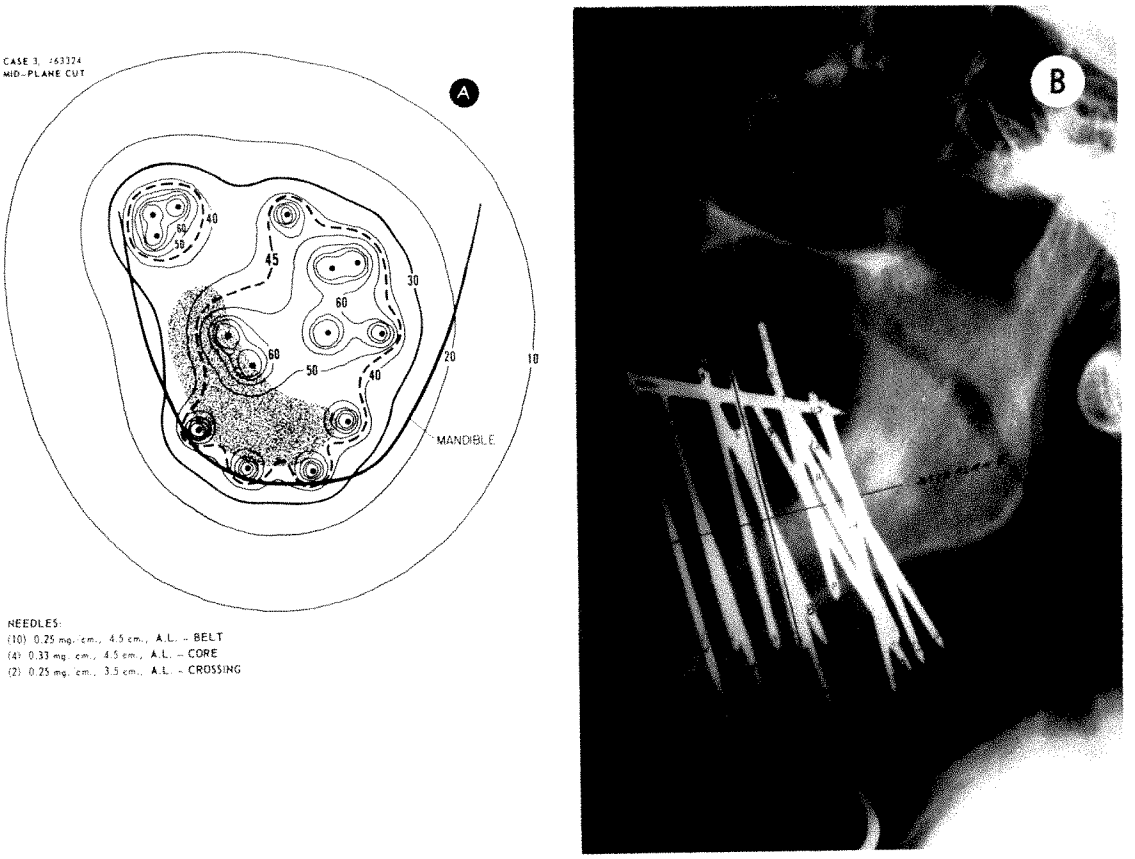


FIG. 4. (*A* and *B*) Midneedle plane of calculation done by the latest version of the program (computer-drawn isodoses). The selected isodose of 45 rads per hour is contrasted with a possible choice of the 30 rads per hour isodose, which would have included considerably more tissue volume and a portion of the mandible.

DISCUSSION

Computer-obtained distributions provide more comprehensive data than the stated dose obtained from Paterson-Parker tables. However, the optimal application of the data requires a consideration of the important clinical factors learned from past experience, including the anatomic site of the lesion, the dose rate, tissue volume receiving the actual minimum tumor dose and location of important adjacent structures.

Our experience has shown that the following parameters are of importance:

1. Attention to recent information regarding dose distribution in implants; for example, in planar implants a more uniform dose is achieved when all the needles are of the same intensity, and a better dose distribution is obtained when double plane implants have a separation of 1.5 cm.

2. The complication rate decreases with low dose rate implants (less than 40 rads per hour) which are easier to accomplish using low intensity (0.25 or 0.33 mg. per cm.) needles throughout the implant.

3. Increasing use of external preneedling irradiation in larger tumors with corresponding adjustment in the time-dose relationships for the radium implant.

4. Less generous selection of minimum tumor dose from computer isodoses. A selection of an isodose curve encompassing all the needles, although a natural first choice, usually leads to overdosage. This is particularly important in implants of the floor of the mouth where the necrosis rate is higher.

5. Attention must be directed to the clinical type of lesion. In infiltrative lesions it may be necessary to risk a necrosis in order to have an acceptable control rate.

6. Continued experience with the computer isodose program is needed. For the reasons enumerated in this paper, the number of rads delivered cannot be directly compared to the Paterson-Parker stated dose or even to dose distributions obtained from other computer programs.

SUMMARY

We have described the development of our interstitial radium therapy computer dosimetry program, including the present system (RADCOMP) together with several representative cases, to illustrate a few of the problems in the clinical application of the computer dosimetric data. Further experience will be needed to determine the most profitable application of computer dosimetry, but it is obvious that clinical judgment must be used to obtain the best results.

Joseph R. Castro, M.D.
Department of Radiotherapy
The University of Texas
M. D. Anderson Hospital
and Tumor Institute at Houston
Houston, Texas 77025

REFERENCES

1. Batten, G. W., Jr. M. D. Anderson method for computation of isodose curves around interstitial and intracavitary radiation sources. II. Mathematical and computational aspects. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1968, *102*, 673–676.
2. Fletcher, G. H., and Stovall, M. Study of explicit distribution of radiation in interstitial implantations. II. Correlation with clinical results in squamous cell carcinomas of anterior two-thirds of tongue and floor of mouth. *Radiology*, 1962, *78*, 766–782.
3. Fletcher, G. H., MacComb, W. S., and Shalek, R. J. Radiation Therapy in the Management of Cancers of the Oral Cavity and Oropharynx. Charles C Thomas, Publisher, Springfield, Ill., 1962.
4. Fletcher, G. H. Textbook of Radiotherapy. Lea & Febiger, Philadelphia, 1966.
5. Meredith, W. J. Editor. Radium Dosage: The Manchester System. E. & S. Livingstone, Ltd., Edinburgh, 1947.
6. Parker, H. M. Dosage system for interstitial radium therapy: physical aspects. *Brit. J. Radiol.*, 1938, *11*, 313–340.
7. Paterson, R., and Parker, H. M. Dosage system for gamma ray therapy. *Brit. J. Radiol.*, 1934, *7*, 592–632.
8. Paterson, R. Studies in optimum dosage. Mackenzie Davidson Memorial Lecture. *Brit. J. Radiol.*, 1952, *25*, 505–516.
9. Paterson, R. The Treatment of Malignant Disease by Radiotherapy. Second edition. Williams & Wilkins Company, Baltimore, 1963.
10. Shalek, R. J., and Stovall, M. Calculation of dose in interstitial implantations. In: Radiation Therapy in the Management of Cancers of the Oral Cavity and Oropharynx. Edited by G. H. Fletcher, W. S. MacComb, and R. J. Shalek. Charles C Thomas, Publisher, Springfield, Ill., 1962.
11. Shalek, R. J., and Stovall, M. M.D. Anderson method for computation of isodose curves around interstitial and intracavitary radiation sources. I. Dose from linear sources. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1968, *102*, 662–672.
12. Stovall, M., and Shalek, R. J. Study of explicit distribution of radiation in interstitial implantations. I. Method of calculation with automatic digital computer. *Radiology*, 1962, *78*, 950–954.
13. Stovall, M., and Shalek, R. J. M.D. Anderson method for computation if isodose curves around interstitial and intracavitary radiation sources. III. Roentgenograms for input data and relation of isodose calculations to Paterson-Parker system. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1968, *102*, 677–687.

CURRENT TECHNIQUES WITH 6–18 MEV. ELECTRON BEAM*

By NORAH DUV. TAPLEY, M.D., *and* GILBERT H. FLETCHER, M.D.
HOUSTON, TEXAS

ON MAY 1, 1963 electron beam therapy was started in the Department of Radiotherapy at the M. D. Anderson Hospital. During the initial phase of application, the 6–18 mev. electron beam provided either the single modality of treatment or additional dosage to a limited volume following comprehensive cobalt 60 teletherapy. With the rapid build-up of the electron beam producing a slight but definite skin sparing and with the sharp fall-off in depth dose beyond the 80 per cent dose level (particularly at lower energies), the technique most often used was a single appositional portal.[2] It was recognized that the homogeneously high dose produced throughout this volume of tissue might lead to excessive injury of the skin and subcutaneous tissues. Analysis of the results of the first 3½ years of treatment with the electron beam has demonstrated, in the normal tissues of some patients, an unacceptable degree of radiation sequelae, both early and late. The purpose of this paper is to review the current techniques of applying the electron beam, which in some situations have been modified but in others have been maintained with little alteration.

UPPER RESPIRATORY AND DIGESTIVE PASSAGES

PRIMARY LESIONS

In the treatment of malignant lesions of the upper respiratory and digestive passages, the 6–18 mev. electron beam was considered suitable to provide the entire treatment for cancers of the oral cavity, in particular the buccal mucosa and the floor of mouth, and for well-lateralized cancers of the oropharynx, particularly lesions of the retromolar trigone and anterior tonsillar pillar. In the hypopharynx, the electron beam was used to treat cancers of the lateral pharyngeal walls, and in the supraglottic larynx, cancers of the aryepiglottic folds and arytenoids. These lesions were treated with a single appositional field, the mev. selected according to the depth of the lesion, with tumor doses of 6,000 rads in 4 weeks for small lesions and up to 8,000 rads in 6½ to 7 weeks for large lesions. In order to deliver these doses to the 80 per cent depth dose, the doses near the surface and for a centimeter or two beyond are as high as 7,500 to 9,500 rads.

If the entire treatment has been given with the electron beam alone, particularly in the head and neck area when a high mev. has been necessary and the doses have been large, the acute skin reactions have been severe and the late changes have been pronounced. Although moist skin reactions have developed in over 50 per cent of the patients treated at 15–18 mev. with given doses of from 7,000 rads in 5 weeks to 8,500 rads in 6½ weeks, healing has been rapid. Table 1 compares the incidence of subcutaneous fibrosis in patients treated with the electron beam alone with those treated with the electron beam combined with other radiation, either photon beam or interstitial radium. The number of patients developing fibrosis when the electron beam is combined with other radiation is significantly lower, particularly in the treatment of lesions of the floor of mouth and of the tonsillar area. When the electron beam is used alone for the treatment of these areas, because of the greater depth, a higher mev. must be used and the total given dose must be larger to achieve the desired tumor dose.

* Presented at the Fiftieth Annual Meeting of the American Radium Society, Miami Beach, Florida, April 7–11, 1968.
From the Department of Radiotherapy, The University of Texas M. D. Anderson Hospital and Tumor Institute at Houston, Houston, Texas.
This investigation was supported in part by U. S. Public Health Service Research Grant CA-06294.

TABLE I

INCIDENCE OF SUBCUTANEOUS FIBROSIS AFTER ELECTRON BEAM THERAPY IN PRIMARY LESIONS OF UPPER RESPIRATORY AND DIGESTIVE PASSAGES

May 1, 1963 to December 31, 1966

Anatomic Sites	No. of Patients Treated	Fibrosis		
		Electron Beam Therapy Alone	Electron Beam Therapy Combined	Electron Beam Therapy Boost
Buccal Mucosa and Gingiva	33	12% (3/25)	14% (1/7)	0% (0/1)
Floor of Mouth	45	22% (4/18)	8% (2/26)	0% (0/1)
Tonsillar Area	91	27% (2/11)	3% (1/31)	14% (7/49)
Hypopharynx and Supraglottic Larynx	32	0% (0/12)	12% (1/8)	8% (1/12)

Additional or "boost" treatment with the electron beam following comprehensive cobalt 60 teletherapy to 5,000 rads to the primary and neck lymph nodes, was given through a limited field to primary lesions, particularly in the anterior tonsillar pillar and the base of tongue. The added dose given with the electron beam resulted in tumor doses of 7,000 rads in $6\frac{1}{2}$ weeks or 8,500 rads in 8 weeks. A significant degree of subcutaneous fibrosis has developed following electron beam boost treatment to these doses, particularly in patients with tonsillar area lesions.

These findings have led to alterations in the application of the 6–18 mev. electron beam in the treatment of primary lesions of the upper respiratory and digestive passages. The current technique of treatment consists of modifications in the proportion of the dose provided by the electron beam and in the total tumor dose administered to the patient. In order to limit the high dose to the skin and subcutaneous tissues and to avoid underdosing which might result from shadowing by bone, the electron beam is frequently combined with high energy photons or with interstitial radium. In the treatment of lesions of the oral cavity, such as the buccal mucosa and the floor of mouth, the tumor dose given with the electron beam rarely exceeds 5,000 rads in 5 weeks and is followed by radium needling, radioactive gold grains, or high energy photons.

The electron beam is most often used in a 1:1 ratio with the photon beam in the treatment of lesions of the tonsillar area and the hypopharynx. With this technique, the intense mucosal reaction with confluent exudate is confined to the homolateral side and the reaction on the contralateral side is limited to erythema without mucosal studding. The later reactions of moderate to severe dryness and loss of taste sense, which commonly occurs with parallel opposing portals, are seen infrequently and to a limited degree with the technique of combined electron and photon beams. Table II gives the results in patients with T1–T3 lesions treated with combined photon and electron beams. They are of the same order as those obtained with the photon beam only (cobalt 60 or megavoltage roentgen ray). The advantage of the technique is provided by the decrease in number and severity of radiation sequelae in the normal tissues. Electron beam boost therapy for primary lesions of the head and neck following 5,000 rads tumor dose with cobalt 60

TABLE II*

RESULTS OF ELECTRON BEAM THERAPY IN PRIMARY CARCINOMA OF THE UPPER RESPIRATORY AND DIGESTIVE PASSAGES

May 1, 1963 to December 31, 1966

Site	No. of Patients	Salvaged with Surgery	Dead with Primary Lesion	Dead with Enlarged Lymph Nodes	Dead with Distant Metastases	Dead with Intercurrent Disease or Other Malignancy	No Evidence of Disease
Buccal Mucosa	20						
No recurrence	14			1	1	1	13 (2 with surgery)
Recurrence	6		1				
Surgery for recurrence	5	2	3				
Gingiva	13						
No recurrence	7					2	8 (3 with surgery)
Recurrence	6		1				
Surgery for recurrence	5	3	1			1	
Floor of Mouth	45						
No recurrence	34			1	2	4	32 (5 with surgery)
Recurrence	11		2				
Surgery for recurrence	9	5	2			2	
Tonsillar Area	91						
No recurrence	74			6	4	7	66 (9 with surgery)
Recurrence	17		5				
Surgery for recurrence	12	9	3				
Hypopharynx and Supraglottic Larynx	32						
No recurrence	23			1	1	5	19 (3 with surgery)
Recurrence	9		4				
Surgery for recurrence	5	3	1			1	

* The above table shows a 19 per cent recurrence rate in T1-T3 tonsillar area lesions treated with the electron beam from May 1, 1963 to December 31, 1963. This control rate of 82 per cent is comparable to the 5 year, local control rate in patients receiving photon beam treatment in this department. Although the follow-up is no more than 1 year in a few patients, 80 per cent of recurrences are seen within 1 year after treatment and 90 per cent within 2 years.

teletherapy rarely exceeds an added tumor dose of 1,500 to 2,000 rads, usually given with combined electron and photon beams. Surgical resection of recurrences following electron beam therapy has been possible without undue delay in healing and has provided a significant salvage rate (Table II).

CERVICAL LYMPH NODE METASTASES

The electron beam, usually at 9 mev., has been used in the treatment of the entire neck with the field defined by a lead cutout. The given doses have been 5,000 rads in 5 weeks prior to radical neck dissection. Following radical neck dissection without preoperative irradiation, when there is a pathology report of tumor cells in connective tissue or a large number of positive lymph nodes, the entire neck is treated at 9 mev. to a given dose of 6,000 rads in 5 weeks. With skin or subcutaneous recurrences after radical neck dissection, if the tumor mass is thicker in one area, 12 mev. has been used in that portion of the field. The given dose is usually 6,500 to 7,000 rads in $5\frac{1}{2}$ to 6 weeks with the last 500 to 1,000 rads given at 9 mev. through a sharply reduced portal to the area of known recurrent disease. Because of the limited volume and lower surface dose (approximately 87 per cent at 9 mev.), severe skin reactions and late subcutaneous tissue changes have not been seen.

Table III gives treatment details and tissue reactions, early and late, in the treatment of the whole neck in 29 patients. Sev-

eral patients have been followed for as long as 47 months. With large fields and exposure doses of 6,000 to 6,500 rads in 5 weeks, the majority of the patients showed a dry reaction only. If the reaction has been moist, it has been limited in extent with a rapid healing time. There have been minimal late skin changes with slight atrophy and telangiectasias. Only 4 patients have shown a mild to moderate degree of fibrosis without associated symptoms. In the treatment of the whole neck, the technique originally developed with the electron beam has not been changed, since a given dose of 6,000 rads in 5 weeks is well tolerated with minimal late reactions in the skin and subcutaneous tissues.

With electron beam boost therapy to cervical lymph node metastases, the added electron beam doses ranged from 2,400 to 3,500 rads following 5,000 to 6,000 rads with cobalt 60 teletherapy, the total dose being as high as 9,000 rads in 8 to 8½ weeks. It was considered that the limited field size and volume treated with the electron beam would permit these high dose levels without a significant increase in the complication rate. Observation of the areas of marked fibrosis in patients receiving these high doses has necessitated modification of the boost technique. The field size for the boost is selected most economically to cover only the residual induration at the site of the original metastatic lymph node mass and the given doses have been decreased to 1,000 to 1,500 rads.

BREAST

PERIPHERAL LYMPHATICS

After radical mastectomy, irradiation of the apex of the axilla, the supraclavicular region, and the internal mammary chain is done if the breast primary lesion is in the inner quadrant or subareolar area, or if there are positive axillary lymph nodes. From May, 1963 to December, 1966 the electron beam has been used in the irradiation of the peripheral lymphatics alone in 64 patients and for irradiation of both the peripheral lymphatics and the chest wall in 31 patients. The apex of the axilla and the supraclavicular area received a given dose of 5,650 rads, 300 rads daily, in 3½ weeks at 12 mev., the tumor dose being 5,000 rads to most lymph nodes. The internal mammary chain received a given dose of 5,650 rads, 300 rads daily, in 3½ weeks at 15 mev., the calculated tumor dose being 5,000 rads at 3 cm. depth.

TABLE III

SKIN AND SUBCUTANEOUS REACTIONS AFTER ELECTRON BEAM THERAPY TO THE WHOLE NECK
May 1, 1963 to December 31, 1966

9 mev.	18 patients
12 or 15 mev.	11 patients
Field Size	140–240 cm.²
Exposure Dose	250 rads, daily; total, 6,000–6,500 rads
Dry Reaction	20 patients
Moist Reaction	9 patients; healing time, 7–20 days
Late Change	Skin, minimal; fibrosis, 4 patients
Follow-up	13–47 months

In 95 patients having received electron beam treatment to the peripheral lymphatics, with the higher energies used to treat the supraclavicular and internal mammary lymph nodes, a patchy, moist desquamation has been seen in approximately one-half of the patients, but the healing time has been rapid. In some patients numerous telangiectasias have developed after several years. Fibrosis in the supraclavicular fossa has been seen in 4 patients (Table IV). Mediastinitis or pneumonitis have not been observed.

Although the late sequelae are not severe, telangiectasias should be avoided. In the treatment of the peripheral lymphatics with the current technique, the total dose to the supraclavicular lymph nodes and to the internal mammary lymph node area is 5,000 rads in 4 weeks, 250 rads given dose daily. The decrease in total dose is considered acceptable following a recent review[1] of the incidence of recurrence of supraclavicular disease which showed that 4,500 rads megavoltage radiation in 4 weeks resulted in 90 per cent control of subclinical disease.

TABLE IV

COMPLICATIONS AFTER ELECTRON BEAM THERAPY FOR CARCINOMA OF BREAST
May 1, 1963 to December 31, 1966

Area Treated	No. of Patients	Complications		
		Fibrosis	Skin Necrosis	Rib Fracture
Peripheral Lymphatics	64	0		
Chest Wall	78	0	6	7
Peripheral Lymphatics and Chest Wall	31	4*	3†	1
Boost to Breast	69	16	10	6
Boost to Axilla	50	12		

* Four patients developed fibrosis in the supraclavicular area field.
† Three patients developed necrosis in the chest wall.

CHEST WALL

The electron beam has been considered particularly suitable in the treatment of the entire chest wall. Following radical mastectomy, the chest wall and peripheral lymphatics are treated with the electron beam if more than 20 per cent of the axillary lymph nodes are positive, or, with negative lymph nodes, when the primary breast tumor involves the skin or is fixed to the underlying structures. The given dose had been 6,000 rads in 4 weeks at 6 or 9 mev., dependent upon the estimated thickness of the chest wall, and encompassing an area up to 400 to 450 cm.^{2}. Similar treatment has been administered for patients presenting with recurrent chest wall nodules following radical mastectomy. In the treatment of the chest wall with large fields and exposure doses of 6,000 rads, moist reactions have been patchy and have healed rapidly. Fibrosis has not been seen in the chest wall, but telangiectasias have become numerous in a moderate number of patients.

Necrosis (Table IV) developed in patients whose treatment was begun prior to complete healing of the mastectomy wound. Because of the observation that unhealed mastectomy wounds tend to remain unhealed for long periods if irradiated, requiring secondary grafting in some instances, treatment is not instituted unless there is complete closure of the surgical incision. With the observation that at 9 mev. a significant incidence of symptomatic radiation pneumonitis occurred, the chest wall is treated at 6 mev. unless the chest wall is demonstrated to be close to 3 cm. in thickness. The total given dose to the large chest wall fields has been decreased to 5,500 rads in 4 weeks, 275 rads daily.

BOOST TREATMENT TO BREAST PRIMARY TUMOR AND LYMPH NODES

The electron beam has been used to provide "boost" therapy to the breast primary tumor and/or the axillary lymph nodes for residual induration following comprehensive treatment with cobalt 60 teletherapy. The given doses with the electron beam have been as high as 3,000 rads in 2 weeks or 5,000 rads in 3½ weeks, providing tumor doses to the primary tumor of 8,500 rads in 11 weeks or 9,500 rads in 13 weeks and to the lymph nodes of 8,000 rads in 11 weeks. These high doses were thought to be feasible because they were given to a limited volume and because of the skin sparing with the electron beam.

The high necrosis rate (Table IV) in the patients receiving boost therapy to the breast primary lesion is considered to be related both to the incidence of existing ul-

cerated lesions and to the high doses which were originally given. Both the degree of fibrosis in these patients and the incidence of necrosis have indicated the desirability of decreasing the boost doses. These patients now receive given doses from 2,100 rads in 10 days to 3,000 rads in 2½ weeks.

SUMMARY

The current techniques with the electron beam are summarized as follows:

1. *Treatment of primary lesions of the upper respiratory and digestive passages.*
   a. Combined photon and electron beams in a 1:1 ratio of given doses.
   b. Interstitial radium or radioactive seeds to complete treatment, after tumor doses of 4,000 rads in 4 weeks or 5,000 rads in 5 weeks are given with the electron beam.
   c. Boost therapy, after 5,000 rads in 5 weeks with cobalt 60 teletherapy, is limited to 1,500–2,000 rads tumor dose with the electron beam alone or combined with the photon beam in a 1:1 ratio, if required by depth or in an area shadowed by bone.
2. *Treatment of cervical lymph node metastases.*
   a. The entire neck, either prior to or following radical neck dissection, is treated with the 9 mev. electron beam. If preoperative, the given dose is 5,000 rads in 4 weeks, if postoperative, the given dose is 6,000 rads in 5 weeks, with a boost of 500 or 1,000 rads for recurrent disease.
   b. Boost therapy to residual lymph nodes, after 5,000 to 6,000 rads with cobalt 60 teletherapy, is limited to 1,000 to 1,500 rads given dose to a sharply reduced field.
3. *Treatment of breast cancer.*
   a. Following radical mastectomy, the peripheral lymphatic areas (supraclavicular and internal mammary) are treated with the 12 and 15 mev. electron beam to a given dose of 5,000 rads in 4 weeks. The chest wall is treated at 6 mev. and receives 5,500 rads in 4 weeks.
   b. Boost therapy to the breast primary lesion and axillary lymph nodes, following comprehensive cobalt 60 teletherapy, is limited to given doses of 1,500 rads in 10 days to 3,000 rads in 2½ weeks to a sharply limited field.

Norah duV. Tapley, M.D.
Department of Radiotherapy
The University of Texas
M.D. Anderson Hospital
and Tumor Institute at Houston
Houston, Texas 77025

REFERENCES

1. Montague, E., White, E., and Fletcher, G. H. Role of radiation therapy in primary management of breast cancer. To be published.
2. Tapley, N. duV., and Fletcher, G. H. Patterns of use of 6–18 mev. electron beam radiation therapy. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1967, *99*, 924–931.

THE DOSIMETRIC AND BIOLOGIC PROBLEMS POSED BY ELECTRON BEAM THERAPY*

By M. TUBIANA
VILLEJUIF, FRANCE

ELECTRON beam therapy is already fairly old,[10,33] in fact almost as old as high energy photon therapy. In the latter case dosimetric and biologic problems have been satisfactorily resolved, whereas for electron beam therapy, even after several symposia, they remain under discussion.

The values for RBE reported by different authors in various biologic materials diverge considerably[10,16,24,26] and cannot be explained on a biologic basis. A problem such as the possible variation of RBE with depth in tissue, which is of basic importance in radiotherapy, has been the subject of several contradictory articles. Some conclude that it is absent[7,22,29] and others that such a variation exists.[14,15,19,28] Most of these inconsistencies seem to us to be related to dosimetric problems.

I. MEASUREMENT OF ABSORBED DOSE

The measurement of absorbed dose can be made directly by calorimetry; however, the method is difficult and rare are the radiotherapy centers which can employ it. If an ionization chamber is used, several correction coefficients are necessary, notably to take into account the polarization effect. In the calculation of these correction coefficients the energy spectrum of electrons traversing the chamber and the characteristics of the chamber must be known.

If corrections are not made, the readings obtained from a commercial ionization chamber can differ by 20–25 per cent with the absorbed dose in rads. The widespread usage of the so called "r Victoreen" is one of the factors which has been most detrimental to the progress of electron beam therapy and to the necessary correlation of results obtained at different treatment centers. It explains equally and to a large extent the variations in RBE obtained from one center to another. This method, which, for the measurement of RBE, consists of a comparison of the biologic effect of a certain number of "r Victoreen" from photon irradiation and of "r Victoreen" from electron beam irradiation, is a notable oversimplification since the photon "r Victoreen" rad differs from the electron "r Victoreen" rad.

Even more difficult dosimetric problems are encountered in the study of RBE at different depths. As the dose varies rapidly with depth, an accurate depth dose curve is required. It is known[11,13,18,21] that considerable differences exist between depth dose curves based on measurements from different types of dosimeters (ionization chamber, films, lithium fluoride, ferrous sulfate, calorimetry, etc.).

This may be particularly attributed to the fact that corrections which vary with the depth at which the chamber is used have to be applied to readings obtained from the chamber which is calibrated to function at a particular depth. This is especially true for the polarization effect which diminishes with electron energy and hence with depth.

Dutreix and Dutreix[5] have shown that depth dose curves constructed in the same phantom using different ionization chambers can differ considerably. This probably is related to the fact that each ionization chamber has its own characteristics and above all to the relative uncertainty of the point to which the measurement should be related; *i.e.*, the depth at which a point sized chamber should be placed to obtain the same reading. This depth is situated between the anterior wall of the chamber and

* Presented at the Forty-eighth Annual Meeting of the American Radium Society, Phoenix, Arizona, April 13–16, 1966.
From Institut Gustave-Roussy, Villejuif, France.

the central electrode but its exact position is uncertain and probably depends on the type of chamber and the characteristics of the beam. An uncertainty of a few mm. in the position of this point where the dose gradient is high can introduce considerable uncertainty in the dose. The limits of variability can be as high as 50 per cent.

It is thus very difficult to construct accurate depth dose curves using an ionization chamber. Similarly, it is difficult to compare depth dose curves of various betatrons or accelerators, obtained by using different ionization chambers, since these probably differ greatly. In addition the correction coefficients which are used can also vary. The comparison is even more difficult if, as is often the case, no correction coefficient is used. Depth dose curves are also influenced by the type of betatron, especially by the nature of scattering foil and the design of the collimator. The energy of the electrons is of a great importance and is in general inaccurately known if the electron beam has not been properly calibrated.

II. CHEMICAL DOSIMETRY

In order to construct the accurate depth dose curves which are especially necessary for the study of RBE in depth it seemed to us that chemical dosimetry using ferrous sulphate would be preferable.[9,22] This technique lends itself particularly well to intercomparisons between different laboratories. If the necessary precautions are taken its reproducibility is of the order of ±1 per cent. The main problem is the exact value of the parameter G (number of molecules transformed by an absorbed energy of 100 ev.). G varies with the energy of the electrons which are used but this variation is very small between 1 and 25 mev. and can at first be neglected. In addition, minor inaccuracies in the value for G are of no importance when intercomparisons are made. The dosimeter solution can be very thin and this minimizes dose heterogeneity occurring as a result of the rapid fall of dose with depth. Furthermore, vessels containing biologic samples can be filled with ferrous sulphate solution.

Table I

RBE of 20 mev. electrons[20,21]

Material	RBE (Ref. 20 mv. photons)
Survival of *E. coli*	0.99±0.03
Survival of yeast (saccharomyces cerevisiae diploid)	0.98±0.08
LD/3c da. mice C_{57} Bl	0.96±0.25
LD/4 da. mice C_{57} Bl	1.02±0.05

This technique has been used at the Institut Gustave-Roussy[29] to study the RBE of an electron beam at different depths, especially those corresponding to the 95, 83, 37, and 24 per cent isodoses, using as the biologic endpoint *E. coli* survival. The experiments were repeated for the 80 and 37 per cent isodose depths using diploid yeast (saccharomyces cerevisiae) which reacts in a more complex way like a two hit target.

No variation of RBE with depth was seen in either case (Table I and II). If such a variation exists it must be less than the accuracy of the method; *i.e.* 5 per cent for the bacteria and 10 per cent for the yeast.

For the same biologic systems, no difference has been found for the biologic effectiveness of Co^{60} gamma rays, 20 mev. photons and 20 mev. electrons (Fig. 1). By comparison with 200 kv. x rays, the RBE for electrons obtained with the two systems was 0.85 and 0.88. These values are similar to those reported in the literature for high energy photons[24] and confirm the conclu-

Table II

RBE of 20 mev. electrons and depth[20]
(Reference at maximum)

Isodose Per cent	Survival of *E. coli*	Survival of Diploid Yeast
95	1.02±0.03	
85	1.01±0.03	1.00±0.05
37	0.99±0.02	0.97±0.11
24	0.98±0.02	

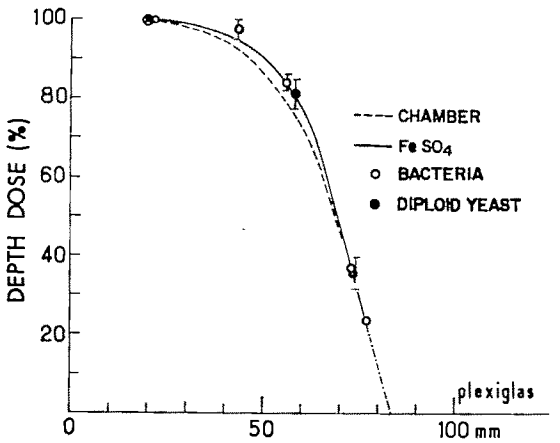


FIG. 1. Diploid yeast survival after irradiation with electron beams at different depths (isodoses 100, 37 and 24 per cent) and with Co^{60} gamma rays.[30]

sion reached by many authors that electrons and photons of similar energy have the same biologic efficiency.

The LD_{50} at 4 days of mice after doses of 900 and 1,300 rads was found to be similar for 20 mev. x rays and 20 mev. electrons (Fig. 2). Thus in the case of intestinal death the ratio of RBE for electrons and the RBE for photons of the same energy is 1.[31] On the other hand, the LD_{50} at 30 days for doses rising from 740 to 900 rads gives a ratio for

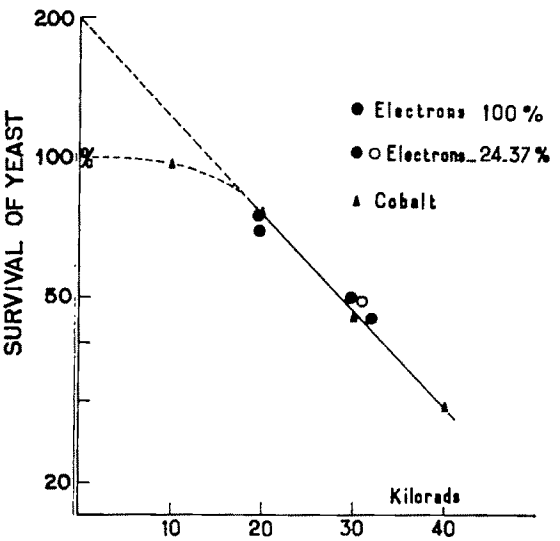


FIG. 2. Depth dose curve determined by ionization chamber (without correction factor), ferrous sulfate, survival rates of *E. coli* and of diploid yeast assuming no variation of RBE with depth.

RBE of 20 mev. electrons and 20 mev. photons of 0.96 ± 0.02 which is significantly less than 1 ($p = 0.01$).[21] Here again it is probably necessary to invoke dosimetric considerations to explain this result.

The dose distribution in the marrow is, under our conditions, more heterogeneous with electrons than with photons. During irradiation the mice are enclosed in lucite boxes and air gaps are present between the wall of the box and the mouse. It is well known that a small air gap causes an appreciable distortion of the dose distribution beyond it, because the probability for the electrons of being scattered in or out of an air-volume is not the same.[1,8,12,18] The electrons tend to concentrate along the edges of the cavity. It has been observed, for instance, that if one introduces bolus into an irradiated field, there is an increased skin reaction along the edge of the bolus which is due to scattered electrons. This can be reduced by rounding the edge of the bolus, but not completely eliminated. The presence of air cavities between the mice and the plastic box may then explain dose variation within the mice. These heterogeneities are small and negligible inside the abdomen, but they may be significant enough in the limbs to explain the lower efficiency of electrons in the case of bone marrow death.

III. DISTORTION OF DOSE DISTRIBUTION IN THE HUMAN BODY

In the human body, air cavities, such as the rhinopharynx or the trachea are responsible for dose heterogeneity but extensive volumes of low density tissue such as the lung are probably the greatest source of distortion of dose distribution.[1,8,12,18] Bone also modifies dose distribution because of its density which is higher than that of soft tissue.

Because the distortion resulting from heterogeneities as well as from irregularities of body contour dose distribution within the human body is difficult to predict, it often is necessary to make use of a heterogeneous phantom. This is of particular ad-

vantage in beam shaping techniques: bolus to reduce the dose to deeply placed organs, screens or scattering foils to protect superficial tissues such as the eye.

Both treatment planning and the interpretation of the results of irradiation are made more difficult by the numerous factors which can alter dose distribution within the organism. The discussion of the results of a recent clinical trial may illustrate this point.

DISCUSSION OF RESULTS OF CLINICAL TRIAL

A few years ago, in view of the differences of opinion which existed about relative therapeutic effectiveness of electrons and photons, it was decided to carry out a controlled clinical trial at the Institut Gustave-Roussy to compare these two types of irradiation. The rate of tumor regression was taken as the criterion of effectiveness, and carcinoma of the tonsil, which could be assessed fairly accurately, chosen as the tumor.

Each patient was examined weekly and independently by three physicians who did not know which treatment was used. The size of the tumor was measured using a code and questionnaire, in as an objective and quantitative way as possible.

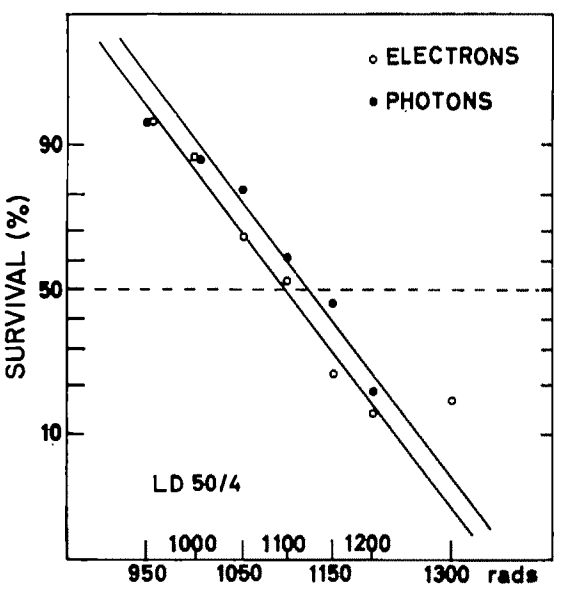


Fig. 3. Mice ($C_{57}Bl$) survival at 4 days after irradiation with electron and photon beams. The difference between the LD_{50} in 4 days is not statistically significant.[31]

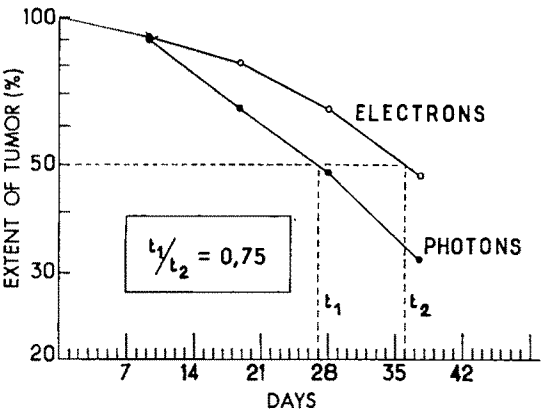


Fig. 4. Evolution of tumor size (expressed as a percentage of the initial size) during irradiation with electron or photon beams. Abscissa: number of days of treatment. The size of the tumors treated with photons is smaller.

Twenty-three patients were treated by 21 mev. x rays and 19 by 20 mev. electrons (Allis-Chalmers Betatron). The two groups were allotted randomly and were statistically comparable. Figure 4 shows that tumor regression was more rapid in patients treated with x rays. The difference is significant. For example, the ratio of days necessary to produce 50 per cent tumor regression by x rays and electrons is 0.75.[7]

The interpretation of the results is, however, very difficult because of dosimetric considerations. We wanted to deliver 250 rads to the target volume at each treatment session. Since initially no dosimeter chamber calibrated for both electrons and photons was available to us, measurements were made on an ionization chamber calibrated for cobalt 60, while we assumed that the calibration coefficients for photons and electrons were the same. In reality, subsequent comparisons using ferrous sulfate dosimetry showed that for the same reading the electron dose was about 5 per cent lower. The dose per treatment was 246 rads for photons and 230 rads for electrons. Thus, the weekly dose being slightly lower in the case of electrons, the time necessary to deliver the same dose was slightly longer.

In order to compare the therapeutic effectiveness of the two types of radiation this fact must be taken into account. This necessitates the construction of a radiobiologic model. This would be easy if the dose-effect relationship for carcinoma of the tonsil were known. As it is not, the consequences of the difference in dose per treatment can only be investigated through the use of models.

If one accepts for example that D_0 is equal to 150 rads and the extrapolation number is 3, it can be calculated that for fractionated treatments of respectively 246 and 230 rads per treatment sessions, the ratio of total doses necessary to kill the same proportion of cells is 0.95 and the ratio of the number of sessions is:

$$0.95 \times \frac{230}{246} = 0.89.$$

In addition, as the average number of sessions per week for patients treated with photons was 3 and for electrons 2.9, the theoretic ratio of the duration of treatment becomes 0.86. Thus the simple difference of dose per treatment and of irradiation frequency can explain the ratio of 0.86 in the isoeffect durations number of treatments by photons and electrons. The observed ratio of 0.75 is lower but the difference is not significant and is compatible with a ratio of RBE for electrons to RBE for photons of 1. This is so because other factors may influence the therapeutic effect of the radiation, particularly the dose distribution within the target volume and peritumoral tissues. These can differ notably with the two types of treatment. Dose heterogeneity within the target volume is another such factor.

The latter may be due to two reasons. The screening effect of the mandible which is relatively easily assessed, and the effect of the air-containing cavities—the buccal and pharyngeal cavities—which is much more difficult to evaluate. In such cavities, the dose disturbance occurs mainly behind the cavity where no lesion is present; however, the dose to the lateral walls may also be modified. The measurements, made *in vivo*, have not shown appreciable deviations from the calculated doses.

In summary, the trial has shown: (1) that it is possible to follow quantitatively the evolution of tumor volume and to use regression as a means of comparing the therapeutic effectiveness of 2 treatments in a relatively small number of cases; (2) that it is important to consider the dosimetric factor, whereby a relatively small difference in dose per treatment session is magnified by the repetition of the sessions; and (3) that the ratio of the RBE for electrons and photons in human tumors is probably close to 1 and is certainly not more.[7]

CONCLUSION

Although electron therapy is one of the most interesting acquisitions of radiotherapy during the past few years, numerous dosimetric problems remain to be solved by various approaches before it can be used routinely in clinical practice: the standardization of a dosimeter which is capable of measuring the absorbed dose in rads with sufficient accuracy; the standardization of beam energy; and the establishment of depth dose curves for treatment conditions. A common language is essential for intercomparisons between various clinical centers.

Treatment planning must take into account the distortions produced by the contour of the patient and tissue heterogeneity. These are often more difficult to predict than with photons, and the use of appropriate phantoms may be necessary for their evaluation.

The ratio of the RBE for high energy electrons to that for 200 kv. x ray is, as for high energy photons, approximately 0.85 and does not appear to vary with depth. This, however, does not mean that a patient can be indiscriminately treated with one or other of these types of radiation, because the relative therapeutic effectiveness may also depend on dose distribution in the target volume and peritumoral tissue which differ from one patient to another. Thus,

controlled clinical trials remain essential in evaluating the benefits which may result in the treatment of various forms of cancer with electron therapy.

Institut Gustave-Roussy
Villejuif 94
France

REFERENCES

1. Boone, M. L. M., Crosby, E. H., and Shalek, R. J. Skin reactions and tissue heterogeneity in electron beam therapy. Part II. In vivo dosimetry. *Radiology*, 1965, *84*, 817–822.
2. Botstein, C., and Schulz, R. J. Experience with high energy electron beam therapy. *Prog. Radiat. Therapy*, 1965, *3*, 27–49.
3. Breitling, G., and Vogel, K. H. Dosisverteilung bei der Bestrahlung inhomogener Medien mit schnellen Elektronen. *Strahlentherapie*, 1963, *122*, 321–340.
4. Cooper, G. W., Van Dyke, J. G., Nickson, J. J., and Laughlin, J. S. Relative biological efficiency of 20 MeV electrons and 250 kevp x-rays as measured in 12 day-old chick embryo. *Radiation Res.*, 1962, *16*, 686–691.
5. Dutreix, J., and Dutreix, A. Étude comparée d'une serie de chambres d'ionisation dans les faisceaux d'électrons de 20 et 9 MeV. *Biophysik.*, 1966, *3*, 249–258.
6. Flamant, R., Malaise, E., Dutreix, J., Hayem, M., Pierquin, B., Tubiana, M., and Dutreix, A. Essai therapeutique controlé sur l'irradiation de cancers amygdaliens par faisceaux de photons ou d'électrons de 20 MeV. *Eur. J. Cancer*, 1967, *3*, 169–181.
7. Fritz-Niggli, H., and Schinz, H. R. Biologische Wirksamkeit von 30 MeV Elektronen in Abhängigkeit von der Gewebetiefe und im Vergleich mit 180 KeV und 31 MeV Photonen. *Strahlentherapie*, 1961, *115*, 379–393.
8. Fritz-Niggli, H., and Schinz, H. R. Biologische Wirksamkeit von 30 MeV Elektronen in Abhängigkeit von der Gewebetiefe und im Vergleich mit 180 KeV und 31 MeV Photonen. II. Lethalitätstest an vierstündigen Drosophilaembryonen. *Strahlentherapie*, 1962, *118*, 503–517.
9. Geisselsoder, J., Koepke, K., and Laughlin, J. S. Calorimetric determination of absorbed dose and GFe ions of Fricke dosimeter with 10 MeV and 20 MeV electrons. *Radiation Res.*, 1963, *20*, 423–430.
10. Haas, L. L., Harvey, R. A., Laughlin, J. S., Beattie, J. W., and Henderson, W. J. Medical aspects of high energy electron beams. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1954, *72*, 250–259.
11. Hettinger, G., Bergman, S., and Osterberg, S. Relative biological efficiency (RBE) of 30 MeV electrons on haploid yeast. *Biophysik*, 1965, *2*, 276–281.
12. Laughlin, J. S., Lundy, A., Phillips, R., Chu, F., and Sattar, A. Electron-beam treatment planning in inhomogeneous tissue. *Radiology*, 1965, *85*, 524–531.
13. Loevinger, R., Karzmark, C. J., and Weissbluth, M. Radiation therapy with high-energy electrons. Part I. Physical considerations, 10 to 60 MeV. *Radiology*, 1961, *77*, 906–926.
14. Markus, B., and Sticinsky, E. Experimente zum Einfluss des Energiespektrums schneller Elektronen auf biologische Reaktionen. *Strahlentherapie*, 1961, *115*, 394–403.
15. Markus, B., and Kolliopoulou, H. Ein qualitativer biologischer Wirkungsunterschied nach Bestrahlung von Teilungsgewebe Energiespektrums. *Biophysik*, 1965, *2*, 263–270.
16. Mookerjee, A., Van Dyke, J. G., and Laughlin, J. S. Relative biological efficiency of 20 MeV electrons and 250 kvp x-rays in saccharomyces cerevisiae inactivation. *Radiation Res.*, 1964, *22*, 431–439.
17. Nagl, J., Sanielevici, A., and Wideröe, R. Calorimetric dose measurements with 35 MeV betatron electron radiation. *Nature*, 1964, *203*, 632–633.
18. Netteland, O. Isodose measurement in inhomogeneous matter. In: Symposium on High-Energy Electrons. Edited by A. Zuppinger and C. Poretti. Springer-Verlag, Berlin, 1965, p. 116.
19. Peters, K., and Breitling, G. Biologische Studien zur Energieübertragung hochenergetischer Elektronen. *Strahlentherapie*, 1963, *122*, 83–90.
20. Report of RBE Subcommittee to I.C.R.P. and I.C.R.U. (1962). *Health Physics*, 1963, *9*, 357–384.
21. Sanielevici, A., and Nagl, J. Kalorimetrische Tiefendosismessungen für 20 MeV Elektronenstrahlung. *Strahlentherapie*, 1965, *127*, 560–565.
22. Schulz, R. J., Schultz, S., and Botstein, C. Clinical and physical aspects of electron beam therapy. *Radiology*, 1963, *80*, 301–303.
23. Shalek, R. J., Sinclair, W. K., and Calkins, J. C. Relative biological effectiveness of 22 Mevp x-rays, cobalt-60 gamma rays and 200 kvcp x-rays. II. Use of ferrous sulfate dosimeter for x-ray and gamma-ray beams. *Radiation Res.*, 1962, *16*, 344–351.
24. Sinclair, W. K., and Kohn, H. I. Relative biological effectiveness of high-energy photons and electrons. *Radiology*, 1964, *82*, 800–815.
25. duV Tapley, N., and Fletcher, G. H. Skin reactions and tissue heterogeneity in electron

beam therapy. Part I. Clinical experience. *Radiology*, 1965, *84*, 812–816.

26. TURANO, L., BIAGINI, C., BOMPIANI, C., and PALEANI-VETTORI, P. G. Radiobiologische, dosimetrische und klinische Grundlagen der Therapie mit schnellen Elektronen eines 15 MeV Betatrons. *Strahlentherapie*, 1959, *109*, 489–504.
27. VERAGUTH, P. Clinical experiments with electron therapy up to 30 MeV. *Brit. J. Radiol.*, 1961, *34*, 152–159.
28. WACHSMANN, F., and KORB, G. Versuche über die Zunahme der biologischen Wirksamkeit schneller Elektronen in der Tiefe. *Biophysik*, 1964, *2*, 11–15.
29. WAMBERSIE, A., DUTREIX, A., DUTREIX, J., LELLOUCH, J., MOUSTACCHI, E., and TUBIANA, M. Efficacité biologique relative d'un faisceau d'électrons de 20 MeV en fonction de la profondeur. *Int. J. Radiat. Biol.*, 1966, *10*, 261–275.
30. WAMBERSIE, A., DUTREIX, A., DUTREIX, J., and TUBIANA, M. Depth dose curves determined by ionization, film density, ferrous sulphate and survival rate of E. coli bacteria and diploid yeast using a 20 MeV electron beam. Symposium on High-Energy Electrons, Montreux, 1964. Edited by A. Zuppinger and C. Poretti. Springer-Verlag, Berlin, 1965, p. 140.
31. WAMBERSIE, A. Thesis. University of Louvain, 1967.
32. ZATZ, L. M., VON ESSEN, C. F., and KAPLAN, H. S. Radiation therapy with high-energy electrons. Part II. Clinical experience, 10 to 40 MeV. *Radiology*, 1961, *77*, 928–939.
33. ZUPPINGER, A. Quelques considerations sur la radiothérapie par les électrons accélérés. *Ann. radiol.*, 1961, *4*, 455–461.

VOL. 105, NO. 1

MODULATION TRANSFER FUNCTIONS OF THE IONIZATION CHAMBER*

By SUGURU UCHIDA, E.D.
OSAKA, JAPAN

DEPTH dosimetry has long been studied by many investigators and a quantity of data are now available, but there are still many problems[4] to be solved.

Above all, the effect[11] of ionization chamber volume on the depth doses is of interest. As for the effect of chamber size on measurements at the edge of an x-ray beam, calculations and experiments have already been reported in detail by Greene[1] and the errors in dosimetry caused by chamber size have been pointed out by him. However, knowledge of the real dose distribution by correcting the errors has remained unsettled, although some analytical approaches to this theme have already been attempted.

The concept of Modulation Transfer Function (MTF),[6,7] which has recently been introduced into the radiographic system with fruitful results in the analysis of images, would contribute greatly to the solution[5] of this question. For one thing, there is the method of correction function described by Jones and Coughlin,[2,3] which aims at elimination of microdensitometer degradation from scans of photographic images. Here, the essential steps in the procedure for microdensitometer correction in transmission space are as follows: (1) to determine the MTF of microdensitometer; (2) to generate a microdensitometer correction function; and (3) to perform a convolution between the correction function and the apparent transmittance data. The actual photographic transmittance data are gained through the above procedure. This is an excellent method which is very skillful and fertile, but the indispensable use of an electronic computer prevents its easy application and popularization.

Accordingly, in this study, for the purpose of solving these questions, the following orthodox method is applied: the problems of the space co-ordinate system are transformed into those of the spatial frequency co-ordinate system and after some treatments are given to these MTFs in the spatial frequency domain, the results are transmitted into the space co-ordinate system by inverse transforms. Thus the solutions are obtained.

The dosimetric system consists of a source, a collimator, a test object (phantom) and a dosimeter. These elements contribute to the blur of the image and they can be treated[5] as a series of linear spatial frequency filters. In this paper, the MTFs of a 4 mm. diameter ionization chamber in dosimetry both in air[8] and in depth[9] will be calculated on some assumptions, and in order to prove these assumptions, the calculations will be compared with the results obtained by some experiments with a lead slit. Furthermore, the dose distribution in air[8] and in depth[9] in the collimated field will be examined by scanning the ionization chamber, and the errors of blurring caused by chamber size will be corrected by means of Fourier analysis in order to obtain the real dose distribution.

The above mentioned experiments were performed using 190 kvp. x rays and Co^{60} γ rays respectively, and the results of these experiments were compared with the energy dependency[10] of the chamber.

THE MTF IN DOSIMETRIC SYSTEM

To begin with, if

$$h(\nu, \tau) = \int_{-\infty}^{\infty}\int_{-\infty}^{\infty} h(x, y) \cdot \exp(-j2\pi(\nu x + \tau y))dxdy, \quad (1)$$

* From the Department of Radiology, Faculty of Medicine, Osaka University, Osaka, Japan.

then

$$h(x,y) = \int_{-\infty}^{\infty}\int_{-\infty}^{\infty} \hat{h}(\nu,\tau) \cdot \exp(j2\pi(\nu x + \tau y))d\nu d\tau \qquad (2)$$

follows, only provided that

$$\int_{-\infty}^{\infty}\int_{-\infty}^{\infty} | h(x,y) | dxdy$$
$$\int_{-\infty}^{\infty}\int_{-\infty}^{\infty} | \hat{h}(\nu,\tau) | d\nu d\tau \qquad (3)$$

is absolutely integrable.

Here, ν, τ are the spatial frequencies in the directions in x-axis and y-axis respectively, and $\wedge$ of $\hat{h}(\nu,\tau)$ indicates Fourier transform of $h(x,y)$.

In general, the MTFs of the radiation dosimetry system are represented in the following way:

Suppose that the depth dose distribution of a field which is formed by collimating the radiation from an extended source is measured with an ionization chamber. A measurement plane is in the fixed position in the phantom, and the depth dose distribution in the measurement plane consists of the depth radiations; *i.e.*, the direct radiation and the scattered radiation. Now let the depth intensity distribution of the measurement plane, which is formed by collimating the radiation from a point source, be $d(x_2, y_2)$ on the co-ordinates of the collimating plane, and let the point spread function of the extended source in the position of the measurement plane in air, and that of the chamber in the depth radiation on the measurement plane be $f(x_1, y_1)$ and $m(x, y)$ respectively, on each of their co-ordinates.

The depth dose distribution $z(x,y)$ which is obtained by examining the field at the measurement plane with the chamber is given by the following convolution integral:

$$z(x,y) = \int_{-\infty}^{\infty}\cdot\cdot\int_{-\infty}^{\infty} d(x_2,y_2)f \cdot(x_1 - x_2, y_1 - y_2)m(x - x_1, y - y_1) \cdot dx_2dx_1dy_2dy_1. \qquad (4)$$

The Fourier transform of Equation (4) as to x, y is

$$\hat{z}(\nu,\tau) = \int_{-\infty}^{\infty}\cdot\cdot\int_{-\infty}^{\infty} d(x_2,y_2)f \cdot(x_1 - x_2, y_1 - y_2)m(x - x_1, y - y_1) \cdot \exp(-j2\pi(\nu x + \tau y))dx_2dx_1dxdy_2dy_1dy = \hat{d}(\nu,\tau)\hat{f}(\nu,\tau)\hat{m}(\nu,\tau). \qquad (5)$$

Therefore, the MTF of the ionization chamber in depth dosimetry is

$$\hat{m}(\nu,\tau) = \frac{\hat{z}(\nu,\tau)}{\hat{d}(\nu,\tau)\hat{f}(\nu,\tau)}. \qquad (6)$$

On the contrary, the real depth dose distribution $r(x, y)$ in the field is to be obtained by the following processes, *i.e.*, if

$$\hat{d}(\nu,\tau)\hat{f}(\nu,\tau) = \hat{r}(\nu,\tau),$$

then

$$\hat{r}(\nu,\tau) = \frac{\hat{z}(\nu,\tau)}{\hat{m}(\nu,\tau)}, \qquad (7)$$

$$r(x,y) = \int_{-\infty}^{\infty}\int_{-\infty}^{\infty} \hat{r}(\nu,\tau) \cdot \exp(j2\pi(\nu x + \tau y))d\nu d\tau. \qquad (8)$$

In air dosimetry, the same analysis is easier, since the phantom is air and the air dose distribution in the measurement plane consists of direct radiation.

CALCULATIONS

The location of points of the ionization chamber is to be represented by a rectangular co-ordinate system, of which the origin is fixed at the center of the chamber, the axes x and y are taken in the directions of the minor and major axes of the chamber respectively, and the axis z righthandedly.

Then the line spread functions and the MTFs of the ionization chamber, for dosimetry in air and in depth, are calculated based on the following assumptions:

Assumption 1. The ionization chamber is assumed to be a cylinder, 2 r in diameter and 2 d in length ($r<d$).

Assumption 2. The ionization current is

assumed to be in direct ratio to any sectional area of the chamber.

Assumption 3. The sensitivity characteristics to radiations are assumed to be uniform in any point in the chamber.

Assumption 4. It is assumed that scattered radiations of uniform energy converging upon one point from all directions are measured by the chamber.

(A) IN AIR DOSIMETRY

The line spread function of the chamber in x-component, $m_1(x)$ is

$$m_1(x) = \int_{-\infty}^{\infty} m(x,y)dy = 2(r^2 - x^2)^{\frac{1}{2}}. \quad (9)$$

The Fourier transform of Equation (9) as to x is

$$\mathfrak{M}_1(\nu) = 2\int_{-\infty}^{\infty} (r^2 - x^2)^{\frac{1}{2}} \exp(-j2\pi\nu x)dx = \frac{r\mathfrak{J}_1(2\pi\nu r)}{\nu}, \quad (10)$$

where $\mathfrak{J}_1$ is the 1st order Bessel function.

The line spread function of the chamber in y-component, $m_2(y)$ is

$$m_2(y) = \int_{-\infty}^{\infty} m(x,y)dx = 1 \quad -d \leqq y \leqq d$$
$$= 0 \quad y < -d, \quad y > d. \quad (11)$$

The Fourier transform of Equation (11) as to y is

$$\mathfrak{M}_2(\tau) = \int_{-\infty}^{\infty} 1 \cdot \exp(-j2\pi\tau y)dy = \frac{\sin 2\pi\tau d}{\pi\tau}, \quad (12)$$

and, if normalized,

$$\frac{\sin 2\pi\tau d}{2\pi\tau d}.$$

(B) IN DEPTH DOSIMETRY

For convenience, various incidence points of scattered radiation in the measurement plane are calculated with the ionization chamber fixed, rather than measuring the scattered radiation converging upon one point by scanning the ionization chamber.

In Figure 1, if θ is an incidence angle which the plane radiation (a sheet of radiations regarded as a plane) vertical to the x-z plane forms with the measurement plane, the line spread function, $m_3(x)$, of the ionization chamber in x-component of the scattered radiation is

$$m_3(x) = 4\int_0^{\pi/2} (r^2 - x^2\sin^2\theta)^{\frac{1}{2}}d\theta, \quad \text{provided} \quad x\sin\theta \leqq r. \quad (13)$$

Equation (13) is an elliptic integral, not solved in general. Therefore, numerical calculations are performed subject to r = 2 mm. and x = 0 $\sim \pm$ 12 mm. The line spread function thus obtained is symmetric, and if Fourier transform is applied, it gives the MTF$\mathfrak{M}_3(\nu)$ of the ionization chamber in x-component of scattered radiation.

$$\mathfrak{M}_3(\nu) = \int_{-\infty}^{\infty} m_3(x)\exp(-j2\pi\nu x)dx. \quad (14)$$

In Figure 2, if θ is an incidence angle which the plane radiation vertical to the y-z plane forms with the measurement plane, and z_1 and $-z_2$ are the values of z of the cross lines of the plane radiation and the bottom of the chamber, the cross area $m_4(y, \theta)$ which the plane radiation with incidence angle θ makes by intersecting the ionization chamber is

$$m_4(y,\theta) = \frac{1}{\sin\theta}\int_{-z_2}^{z_1} (r^2 - z^2)^{\frac{1}{2}}dz = \frac{1}{2\sin\theta}\left[z(r^2 - z^2)^{\frac{1}{2}} + r^2\sin^{-1}\frac{z}{r}\right]_{-z_2}^{z_1}. \quad (15)$$

Z_1 and z_2 have the following values according to θ respectively,

(1) $0 \leqq \theta \leqq \tan^{-1}\dfrac{r}{d+x}$:

$$z_1 = (d - x)\tan\theta$$
$$z_2 = (d + x)\tan\theta$$

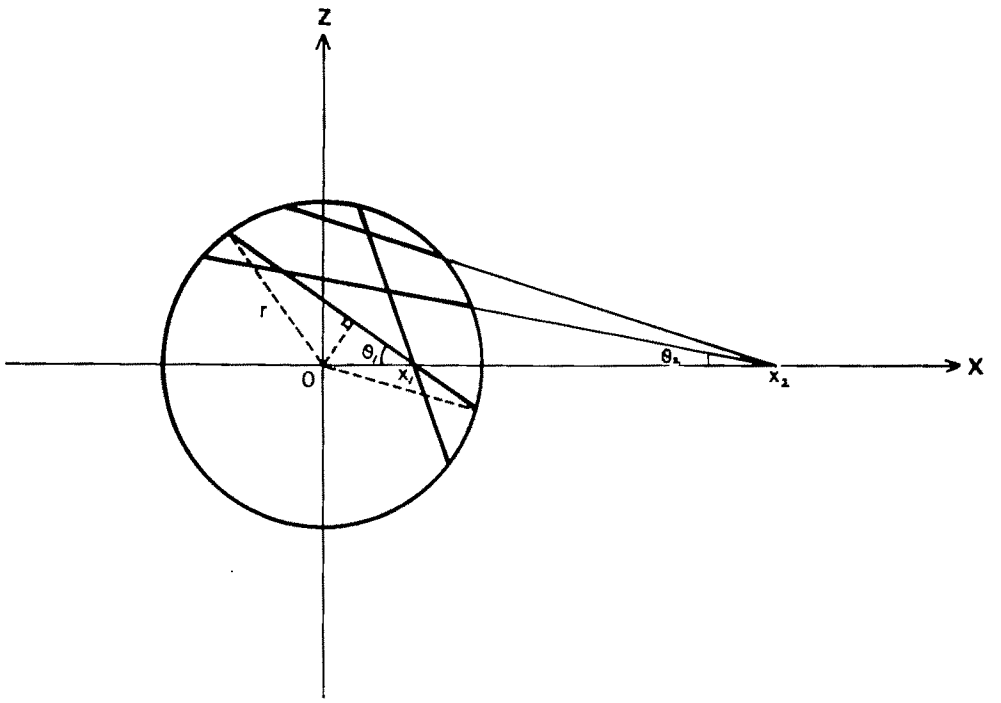


FIG. 1. Reference diagram for calculations of the line spread function of the ionization chamber in x-component of the scattered radiation.

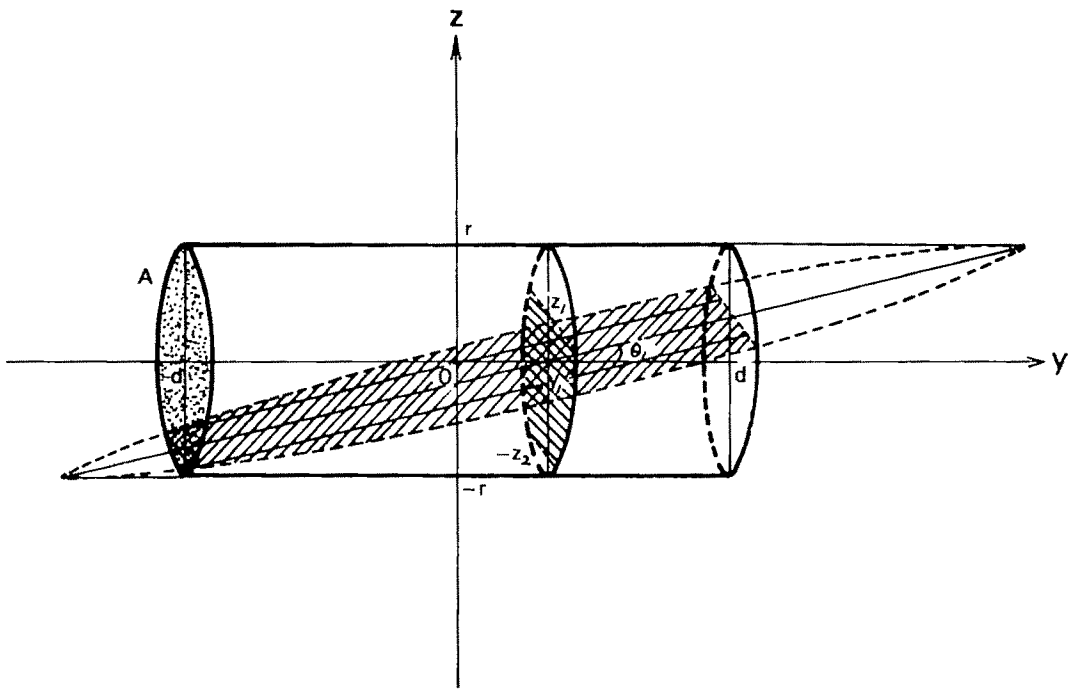


FIG. 2. Reference diagram for calculations of the line spread function of the ionization chamber in y-component of the scattered radiations.

$$(2)\quad \tan^{-1}\frac{r}{d+x} \leqq \theta \leqq \tan^{-1}\frac{r}{d-x}: \qquad (16)$$

$$z_1 = (d-x)\tan\theta$$
$$z_2 = r$$

$$(3)\quad \tan^{-1}\frac{r}{d-x} \leqq \theta \leqq \frac{\pi}{2}: \quad z_1 = r$$
$$z_2 = r,$$

where, it is assumed that the incident radiation does not enter from the bottom A, because it connects with the stem. Therefore, excepting the nonionized rectangular part produced by the radiation being prevented by the bottom A, the ionized area should be corrected separately. Line spread function $m_5(y)$ in y-component of the scattered radiation is

$$m_5(y) = 2\int_0^{\pi/2} m_4(y,\theta)d\theta. \qquad (17)$$

Numerical calculation of Equation (17) is performed subject to d=8 mm., y=0$\sim$ $\pm$48 mm.

The obtained line spread function is slightly asymmetric, and the MTF$\hat{m}_5(\tau)$ of the ionization chamber in y-component of the scattered radiation is given by the Fourier transform of Equation (17).

$$\hat{m}_5(\tau) = \int_{-\infty}^{\infty} m_5(y)\exp(-j2\pi\tau y)dy. \qquad (18)$$

EXPERIMENTS AND RESULTS

The radiations used were x rays and γ rays. In the experiments with the x rays, the apparatus employed was operated for revolving convergent irradiation at 200 kvp., 25 ma., with a constant rate and a Greinacher rectified constant voltage. The tube provided wide angle irradiation with a collimator.

The ionization chamber, the double structure of which is shown in Figure 3, is composed of an outer 10 mm. diameter cylinder with a 5 mm. radius hemispheric head and an inner 4 mm. diameter cylinder

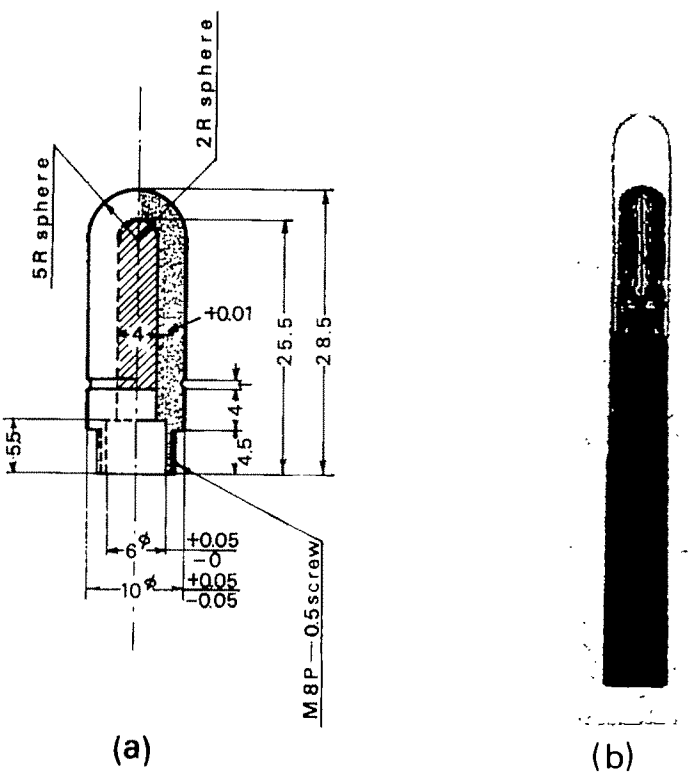


Fig. 3. (*a*) Schematic diagram of the 4 mm. diameter ionization chamber. (*b*) Roentgenogram of the 4 mm. diameter ionization chamber.

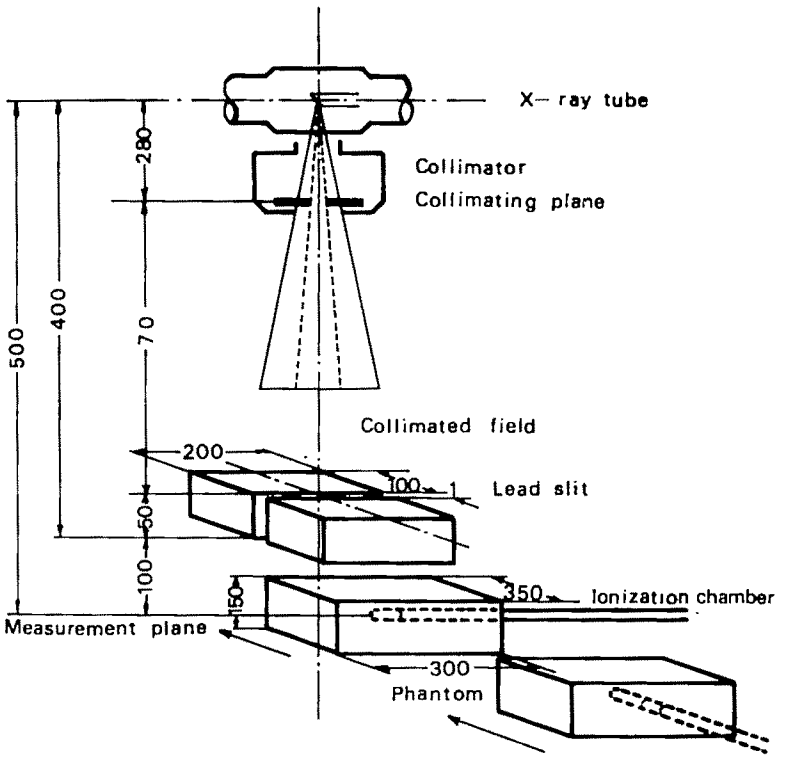


FIG. 4. Schematic diagram of the experimental arrangement.

with a 2 mm. radius hemispheric head. The inner cylinder is filled with air and the outer one with an air equivalent material. The volume of air in the inner cylinder is about 0.2 cc.

The factors of the experimental conditions were as follows: 190 kvp. (half value layer 1.3 mm. Cu); 25 ma.; and a scanning velocity of the ionization chamber of 9.23 mm./min. The lead slit was 200 mm. long by 1 mm. wide, and was made by combining two 50 mm.×100 mm.×200 mm. lead bricks. In the experiments of depth dosimetry, as is shown in Figure 4, the ionization chamber was fixed in the center of a 150 mm.×350 mm.×300 mm. acrylic phantom.

In the experiments with the γ rays, the source was 2,000 c Co^{60} (1.17, 1.33 mev.) and the apparatus a Co^{60} unit for revolving convergent irradiation. The lead slit was 200 mm. long by 1 mm. wide, and was made by combining two 100 mm.×100 mm.×200 mm. lead bricks. The other experimental factors were the same as those used with the x rays.

Figure 4 shows the experimental method of x-ray dosimetry in depth. In air dosimetry, the experimental method is the same as that in depth dosimetry, except that no acrylic phantom is used. In experiments of γ-ray dosimetry in air and in depth, too, the experimental factors are the same as those in x-ray dosimetry except that the source is different.

In the following, the experimental method of x-ray dosimetry in depth is described briefly.

The slit and the major axis of the x-ray tube must be fixed parallel to each other in the position indicated in Figure 4. The x-ray flux is measured by scanning horizontally the ionization chamber in the acrylic phantom in the direction indicated, with its y-axis held parallel (solid line) or rectangularly (dotted line) to the slit. At this time, the scanning distance of the ionization chamber is 24 mm. in the direction of

x-axis with the x-ray flux at its center and 96 mm. in the direction of y-axis, and Fourier transforms are applied to the line spread functions thus obtained. These MTFs are the product of the MTFs of the chamber in x-component or y-component of the depth radiation in the measurement plane, of the depth dose distribution of the x rays through the slit in the measurement plane and of the focus in the position of the measurement plane in air.

Next, the chamber is removed from the phantom, the vacancy is filled with acryl of the same quality, and an x-ray film is placed where the ionization chamber was. Then, the line image density distribution produced by the irradiating x rays on it is measured with a microphotometer. After the density distribution is restored to the intensity distribution with the aid of the film characteristic curve obtained by the experiment in the same acrylic phantom, Fourier transform is applied to it. This MTF indicates the product of the MTF of the focus and that of the distribution of the x rays through the slit. As evidenced by

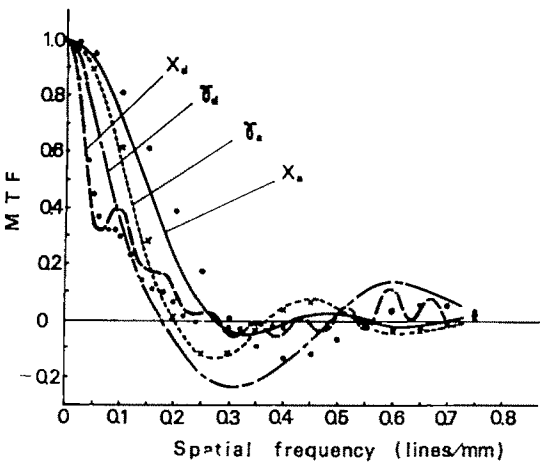


Fig. 5. Comparison between calculations and experiments of the MTFs of the ionization chamber in x-component. X_a: In air dosimetry of x rays. γ_a: In air dosimetry of γ rays. X_d: In depth dosimetry of x rays. γ_d: In depth dosimetry of γ rays. ○: MTFs calculated of the 4 mm. diameter chamber in air. ×: MTFs calculated of the 6 mm. diameter chamber in air. ●: MTFs calculated of the 4 mm. diameter chamber for the scattered radiation.

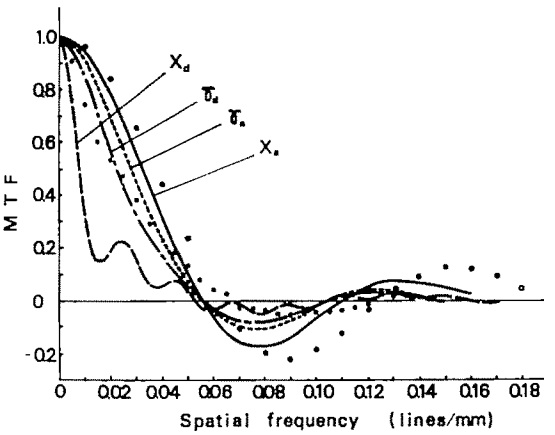


Fig. 6. Comparison between calculations and experiments of the MTFs of the ionization chamber in y-component. X_a: In air dosimetry of x rays. γ_a: In air dosimetry of γ rays. X_d: In depth dosimetry of x rays. γ_d: In depth dosimetry of γ rays. ○: MTFs calculated of the 2 d=16 mm. sized chamber in air. ●: MTFs calculated of the 2 d =16 mm. sized chamber for the scattered radiation.

Equation (6), the MTFs of the ionization chamber in x-component and in y-component of the depth radiation in the measurement plane are easily obtained by a simple division (Fig. 5 and 6). Furthermore, the numerical results obtained by the calculations with Equations (14) and (18) are each plotted.

Then, the lead slit is removed, the collimator adjusted, a slit field of 40 mm. width is formed, parallel to the major axis of the x-ray tube, in the measurement plane, and the dose distribution of the field which consists of the depth radiation is measured in the same way as when the lead slit was used. The scanning distance of the ionization chamber is 80 mm. with the center of the field at its center. From the MTF of this distribution, $f(\nu, \tau)$ is to be calculated by means of Equation (7), and thus the Fourier transform of the real dose distribution in the field consisting of the depth radiation is obtained. The inverse Fourier transform by the numerical integration following Equation (8) is the only one left to be done; *i.e.*, the real depth dose distribution of the field is to be found.

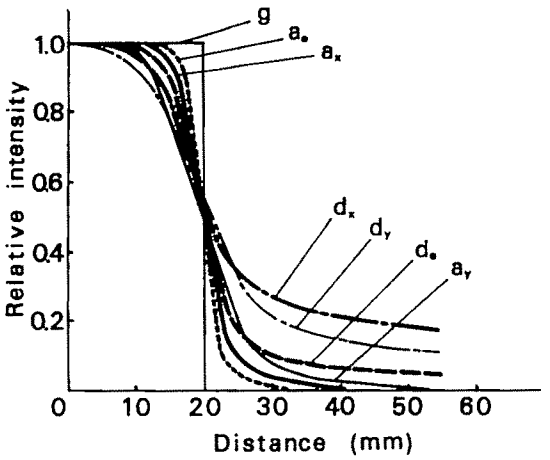


FIG. 7. In the x-ray dosimetry, the dose distribution in the field of 40 mm. width, calculated from the MTFs of the fields by inverse Fourier transforms. a_x: The apparent dose distribution, the dose distribution of the field affected by the blur caused by the focus and by the chamber in the direction of x-axis in air dosimetry. a_y: The apparent dose distribution in the direction of y-axis in air dosimetry. d_x: The apparent dose distribution in the direction of x-axis in depth dosimetry. d_y: The apparent dose distribution in the direction of y-axis in depth dosimetry. a_o: The dose distribution of the field affected by the blur caused by the focus; *i.e.*, desired real dose distribution in air dosimetry. d_o: The real dose distribution in depth dosimetry. g: Geometric dose distribution of the field.

Figure 7 indicates the dose distributions in air and in depth in the x-ray field and Figure 8 those in the γ-ray field.

DISCUSSION

Let us discuss the results shown in Figures 5 and 6 in the light of the four assumptions. Several per cent errors are found between the calculated results in Assumption 1 from Equations (10), (12), (14) and (18) and the MTFs calculated from the real shape. Assumption 2 might be regarded as valid since the ionization current is in direct ratio to the ionization volume. Assumption 3 is daring. Actually the sensitivity to radiation is not uniform at every point in the ionization chamber, which can be observed, for example, in the results shown in Figures 5 and 6.

In Figure 5, as is noted from the comparison of curve X_a with the values calculated subject to 2 r=4 mm. and 2 r=6 mm., the experimental results (curve X_a) are apt to be close to the former (2 r=4 mm.) in low frequency and to the latter (2 r=6 mm.) in high frequency. This implies that, in the line spread function, the experimental results will be close to the calculated ones of the 4 mm. diameter chamber in the low dose domain and of the 6 mm. diameter chamber in the high dose domain. This shows that the chamber center with its stem is better than any other part in sensitivity to x rays. The fact that, in the low frequency domain, the measured results are more towards the lower level than the calculated ones (2 r=4 mm.) is due to the ionizing effect of the air equivalent material in the chamber. In Figure 6, in comparison of curve X_a with the values calculated subject to 2 d=16 mm., the MTFs shown by the actual chamber are, on the whole, of only slightly lower frequency than the calculated re-

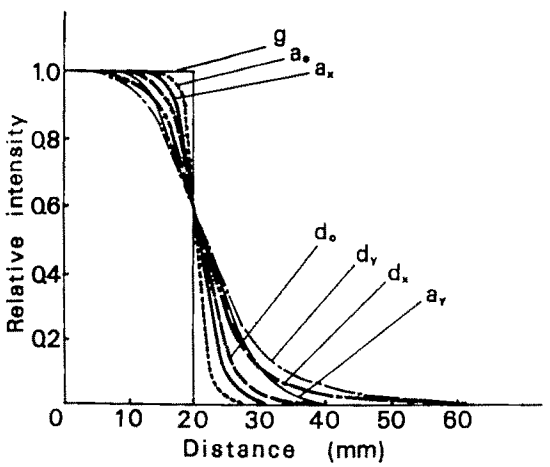


FIG. 8. In the γ-ray dosimetry, the dose distribution in the field of 40 mm. width, calculated from the MTFs of the fields by inverse Fourier transforms. a_x: The apparent dose distribution, the dose distribution of the field affected by the blur caused by the focus and by the chamber in the direction of x-axis in air dosimetry. a_y: The apparent dose distribution in the direction of y-axis in air dosimetry. d_x: The apparent dose distribution in the direction of x-axis in depth dosimetry. d_y: The apparent dose distribution in the direction of y-axis in depth dosimetry. a_o: The dose distribution of the field affected by the blur caused by the focus; *i.e.*, desired real dose distribution in air dosimetry. d_o: The real dose distribution in depth dosimetry. g: Geometric dose distribution of the field.

sults; therefore it may be concluded that the sensitivity characteristics are uniform in the direction of y-axis. The slightly poorer results are due chiefly to Assumption 1 and the experimental errors.

In Figure 5, curve γ_a is more towards the lower level than curve X_a in regards to MTFs, and the chamber becomes larger in its effective size, since the MTF is in good agreement with the values calculated subject to 2 r=6 mm. In the MTFs of the chamber in Figure 6, curve γ_a nearly agrees with curve X_a, little difference being noted in the values of their MTFs.

These results are thought to be due to the ionization of the air equivalent material being more active than that produced by the x rays, since Co^{60} γ rays are of higher energy. Therefore, it appears that Assumption 3 for calculations is satisfactory in the case of Co^{60} γ-ray dosimetry in air.

Assumption 4, that the depth doses in the measurement plane are composed of uniform scattered radiation, is more or less problematic in the case of this experiment in the depth radiation which consists of direct and scattered radiation. The assumption is even more problematic because the scattered rays approach the direction of the direct rays at high energy.

One may not be too bold to think that Assumptions 3 and 4 are approximately satisfied as regards the x-component of the chamber, since the values calculated subject to 2 r=4 mm. are, as shown in Figure 5, in good agreement with curve X_d and largely separated from curve X_a. In comparing curve X_d in Figure 6 with the values calculated subject to 2 d=16 mm., the MTF which the actual chamber shows moves more towards the lower level than the calculated results in the low frequency domain. This implies that, in the line spread function, the scattered x rays, considered a flare in the low dose domain, are over-measured. Similar to curve X_a in Figure 5, this shows that the chamber center with its stem is better than any other part in sensitivity to x rays. Consequently, Assumption 3 is not satisfactory. The calculated values come nearer to curve X_a than in Figure 5. This indicates that the calculated values of the scattered x rays do not differ largely from those in air despite their playing a great part in the calculations. If Assumption 3 is satisfied, curve X_d ought to be approximating the calculated values, just as in Figure 5, and so Assumption 4 is likely to be nearly satisfied.

Regarding Assumption 3, as to the MTFs of the chamber in x-ray dosimetry in air and in depth, the cause of the difference between the values of measurements and those of calculations is the same in either case, but concerning x-axis and y-axis quite a contrary tendency is observed. This is because the paths of x-ray incidence into the chamber are different.

In comparing curve X_a with curve X_d either in Figure 5 or in Figure 6, the curve X_d moves remarkably more towards the lower level than curve X_a in MTF in the low frequency domain, and it allows us to see how poor the characteristics of the chamber become by the flare of the scattered x rays.

In the Co^{60} γ-ray dosimetry in depth, the MTF of the ionization chamber approaches that in the air dosimetry, because the side scattered radiation decreases considerably, while the forward radiation increases, compared with that in x rays. Both curve γ_d in Figure 5 and in Figure 6 lose their oscillations and, moreover, the values of the MTF become larger than those of curve X_d due to the effect of the ionization of the air equivalent material. The difference between the MTFs of the curves γ_a and γ_d is not so large as that in x rays. For this reason, it may be said that Assumption 4 is not satisfactory in this case.

Here, the spurious resolutions are of interest. The phenomenon of spurious resolution by the ionization chamber has been observed in the dosimetric system, although the existence of spurious resolutions by the focus[6] and the motion[7] in the radiographic system is already known. In the measurement of the dose distributions of periodic structure, careful precautions should be taken.

As regards the degree of the spurious resolutions, in Figure 5, curve X_d is little different from curve X_a, in Figure 6, curve X_d is less smooth than curve X_a. This is because the edge in line spread function is made smooth by the scattered x rays, in the direction of y-axis of the chamber. The MTFs of the curves γ_a and γ_d in Figure 5 are larger than those in x rays in the degree of the spurious resolutions. This is probably because the line spread function becomes closer to a rectangle, as the result of the ionization of the air equivalent material being more active, and the side scattered radiation becoming less and the forward one more. In Figure 6, the degree of the spurious resolutions of the MTFs decreases in the following order: the curve X_a, the curves γ_a and γ_d, and the curve X_d. For the same reasons as in Figure 5, it may be concluded that the edge in the line spread function becomes gradually smooth from a rectangle and, in the curve X_d, the effect of flare is produced by the side scattered x rays.

The comparison between curve d_x or d_y and curve d_o in Figure 7 reveals that, in the measurement of the scattered x rays, the doses are measured more in the curve d_x than in the curve d_y. This can be easily explained by the fact that the ionization chamber is a cylinder. Consequently, in the depth dosimetry, we should bear in mind that the dose distribution acquired in the x-component is closer to the real one than in the y-component, while the scattered x rays are measured in larger quantities. In comparing curve a_x or a_y with curve a_o, it is natural that curve a_x should indicate values closer to curve a_o than curve a_y.

Figure 8 indicates that curve d_o becomes only a little smoother than curve a_o, and in γ-ray dosimetry in depth, the side scattered radiation is almost negligible, compared with that in x rays. The rest also is natural.

In Figures 7 and 8, each curve g shows the dose distribution in the geometric field. It makes us see how much an effect the blurring caused by focus size and scattered radiation has on the determination of the field.

In Fourier analysis in this study, particular attention was paid to the following matters in order to secure the accuracy of calculations:

In the Fourier transforms, as stated before, the author increased the scanning distance by 6 times the chamber size and by twice the field width.

In the inverse Fourier transforms, he intended to increase the accuracy of calculations by making the frequency band sufficiently wide.

In getting the experimental results in Figures 5 and 6, it was found that the film dosimetry, in which the measurement of dose distribution in air and in depth of the radiation through the slit in the measurement plane was performed, encounters many problems, and that above all the error in measurement of oblique incident radiations is great. However, one may be allowed to think that this remains within the experimental error.

The author would like to conclude this discussion by making a proposal for the improvement of the ionization chamber.

Nowadays, as a trend in the production of the ionization chamber, various trials are made to make its size as small as possible. A small-sized chamber of high precision is both hard to manufacture and unstable.

In the depth dosimetry, if the chamber diameter is made smaller to raise the accuracy, the length must be greater to secure the sensitivity, and consequently the scattered radiation is overmeasured. For these reasons, it is advisable that the chamber should be precise and stable, even if rather large-sized, since the blurring caused by chamber size in dosimetry can be eliminated by the method of Fourier analysis.

SUMMARY

The blur in the measurement system is analyzed by bringing into the dosimetric system the concept of Modulation Transfer

Function (MTF) which has recently been introduced into the radiographic system with fruitful results in the analysis of images.

In this paper, the dosimetry, in air and in depth, of 190 kvp. x rays and Co^{60} γ rays is treated, respectively.

First, the values of calculations and experiments of MTF of an ionization chamber are obtained. Then, the MTFs of the dose distribution of the collimated field measured by the ionization chamber are obtained.

After some treatments are given to these MTFs in the spatial frequency domain, the real dose distribution of the field is evaluated by inverse Fourier transforms. The results of experiments obtained are discussed in the light of the assumptions for calculations.

Thus by the method of Fourier analysis, it has become possible to know the real dose distribution by correcting the errors of blurring caused by the chamber size, although this has long been regarded as difficult. Therefore, the application of Fourier analysis is tried not only to obtain the expression of MTF of the ionization chamber, but, to go a step farther, and to also measure the real dose distribution.

Suguru Uchida, E.D.
Department of Radiology
Faculty of Medicine
Osaka University
Osaka, Japan

The author would like to express heartfelt thanks to Dr. Hiromu Tachiiri, Professor of Osaka University for his understanding and warm encouragement given to this study and also to Kaoru Morikawa, B.E., Masayuki Maeda, B.E., technical officials of Osaka University and to Hiroshi Ito, B.Sc., Wakayama Workmen's Hospital for their obliging assistance in the experiments.

REFERENCES

1. Greene, D. Observations on effect of chamber size on measurements at edge of x-ray beam. *Brit. J. Radiol.*, 1962, *35*, 856–860.
2. Jones, R. A., and Coughlin, J. F. Elimination of microdensitometer degradation from scans of photographic images. *App. Opt.*, 1966, *5*, 1411–1414.
3. Jones, R. A. Automated technique for deriving MTF's from edge traces. *Phot. Sc. England*, 1967, *11*, 102–106.
4. Kimura, I. Problems in dosimetry. *Jap. J. Radiol. Tech.*, 1963, *19*, 1–38.
5. Uchida, S., Hayami, A., Yamasaki, T., and Azuma, I. Fourier analysis of dosimetric system. Society of Radiation Image Information, 1965, 4–7.
6. Uchida, S. Fourier analysis of x-ray tube focal intensity distribution along beam through optical system. *Oyo Buturi*, 1965, *34*, 97–107.
7. Uchida, S. Fourier analysis of blur of images in layer radiography. *Oyo Buturi*, 1966, *35*, 708–722.
8. Uchida, S. Fourier analysis of blurring caused by ionization chamber. I. In air dosimetry. *Jap. J. Appl. Phys.*, 1968, *7*, 90–91.
9. Uchida, S. Fourier analysis of blurring caused by ionization chamber. II. In depth dosimetry. *Jap. J. Appl. Phys.*, 1968, *7*, 91–92.
10. Uchida, S. Fourier analysis of blurring caused by ionization chamber. III. Concerning energy dependency. *Jap. J. Appl. Phys.* To be published.
11. Yamada, K., Takiuchi, M., and Kimura, I. Consideration on depth dose measurement. *Jap. J. Radiol. Tech.*, 1965, *21*, 1–10.

THE EFFECTS OF PARTIAL IRRADIATION ON TAIL REGENERATION IN ADULT *SIREDON MEXICANUM**

By V. V. BRUNST, Sc.D.
BUFFALO, NEW YORK

STUDY of the effects of radiation in the boundary zone of the irradiation field is of especial interest in radiobiology, because those effects may be related to the stimulating or carcinogenic effects of radiation. On the other hand, study of the regeneration process is of interest, not only in biology but also in medicine, because the problem of regeneration may be related to that of cancer. The regeneration process is similar, in some extent, to tumor formation, since both involve intensive local growth in the adult organism. The usual result of regeneration, however, is a replacement of the amputated portion of the body with a normal structure. Even so, the results of regeneration may sometimes include abnormal growth and the formation of tumor-like structures.

Study of the effects of various external factors on the process of regeneration not only adds significantly to our knowledge of the biologic properties of those factors, but also offers valuable information concerning the process of regeneration itself. Regeneration under adverse conditions, for instance, may disclose unusual potentialities of the regeneration blastema, potentialities that cannot be observed under ordinary conditions.

Among the various external factors that can be applied to the regeneration process, radiation is especially useful, because it is able to penetrate deeply into cells, tissues, and organisms without necessarily creating any immediately visible break in natural barriers, and yet it has the capability of inducing the living material that it reaches to undergo appreciable changes in structure or function. Even when it suppresses mitosis, growth, and development, radiation does not always destroy viability; irradiated tissues sometimes live a very long time.[4]

It is a well established fact that irradiation can inhibit regeneration.[1,4,10,16–22] It is also a well established fact that irradiation-induced inhibition of regeneration is permanent. In *Triton cristatus*, for example, the limbs on one side of the body were irradiated locally, then the limbs on both sides were repeatedly amputated during the next 5 or 6 years (those of some animals 3 times, and those of others 4, 5, 6, or even 7 times); regeneration of the unirradiated limbs was completely normal, but the irradiated limbs were never observed to undergo any regeneration whatever.[15]

All of the amputations of irradiated limbs in the study just cited had been irradiated in full. What would have happened in the case of an amputation in a region proximal enough to have been irradiated only in part? Here a broad spectrum of results would be possible, depending upon such factors as the relative number of damaged and undamaged cells, the nature of the damage in the damaged cells, and the severity of that damage.

As a rule, radiation does not affect all cells within the exposed field equally, since the energy supplied by radiation is discontinuous.[25] Thus a very small dose of radiation is sufficient to kill a few of the cells in a specified area of tissue, but a very large dose is necessary to kill all of the cells in that area. The discontinuous effects of radiation are particularly evident along the borders of the irradiated field, where scattered rays strike some cells but not others.

The present investigation is a morpho-

* From the Radiobiology Laboratory, Roswell Park Memorial Institute (New York State Department of Health), Buffalo, New York.

logic study of regenerates that developed from the boundary zone peripheral to the field of irradiation. In the great majority of cases, amputation was within the irradiated field, where regeneration was suppressed completely; but in the small number of remaining cases, amputation was in the boundary zone, where partial irradiation interfered with regeneration to such an extent that all regenerates were more or less monstrous.

MATERIALS AND METHODS

In 2 series of experiments (A-65 and D-65), the tails of 115 adult axolotls (*Siredon mexicanum*) from 2 different spawnings were amputated, and the regenerates that developed were irradiated locally 1 to 2 months later with one or another of the following doses: 1,000 r, 2,000 r, 4,500 r, and 6,000 r. Irradiation conditions were as follows: 250 kv., 30 ma., 0.25 mm. Cu+1 mm. Al filter, beryllium window tube; half-value layer of 0.95 mm. Al; target-to-object distance 20 cm.; and 1,122 r/min. in air.

Before irradiation the animals were anesthetized with a dilute aqueous solution of tricaine methanesulfonate (MS-222), a special agent designed for immobilizing cold-blooded animals, and were kept in water in a plastic tray. Body areas not to be irradiated were shielded by a lead covering made from a sheet of lead 4 mm. thick, with a round radiation localizer 6.5 cm. in diameter.[5] During irradiation the animals were arranged radially within a circle; immediately afterward, they were returned to individual containers supplied with fresh water.

A more proximal amputation of the tails of the 115 animals was performed a relatively long time (495 to 539 days) after irradiation. The material thus obtained was fixed in Stieve's acetic acid solution of mercuric chloride and formaldehyde.[23] After decalcification with 0.5 per cent HCl in 80 per cent alcohol, specimens were embedded in paraffin containing 5 per cent beeswax, and were sectioned at 8 μ. The sections were stained with Ehrlich's hematoxylin and eosin, and photomicrographs were made with most at $\times$ 42, but occasionally at $\times$ 170 or $\times$ 570.

All of these experimental and preparative methods, except those concerned with irradiation, were also applied to 20 unirradiated animals from the same spawnings.

RESULTS

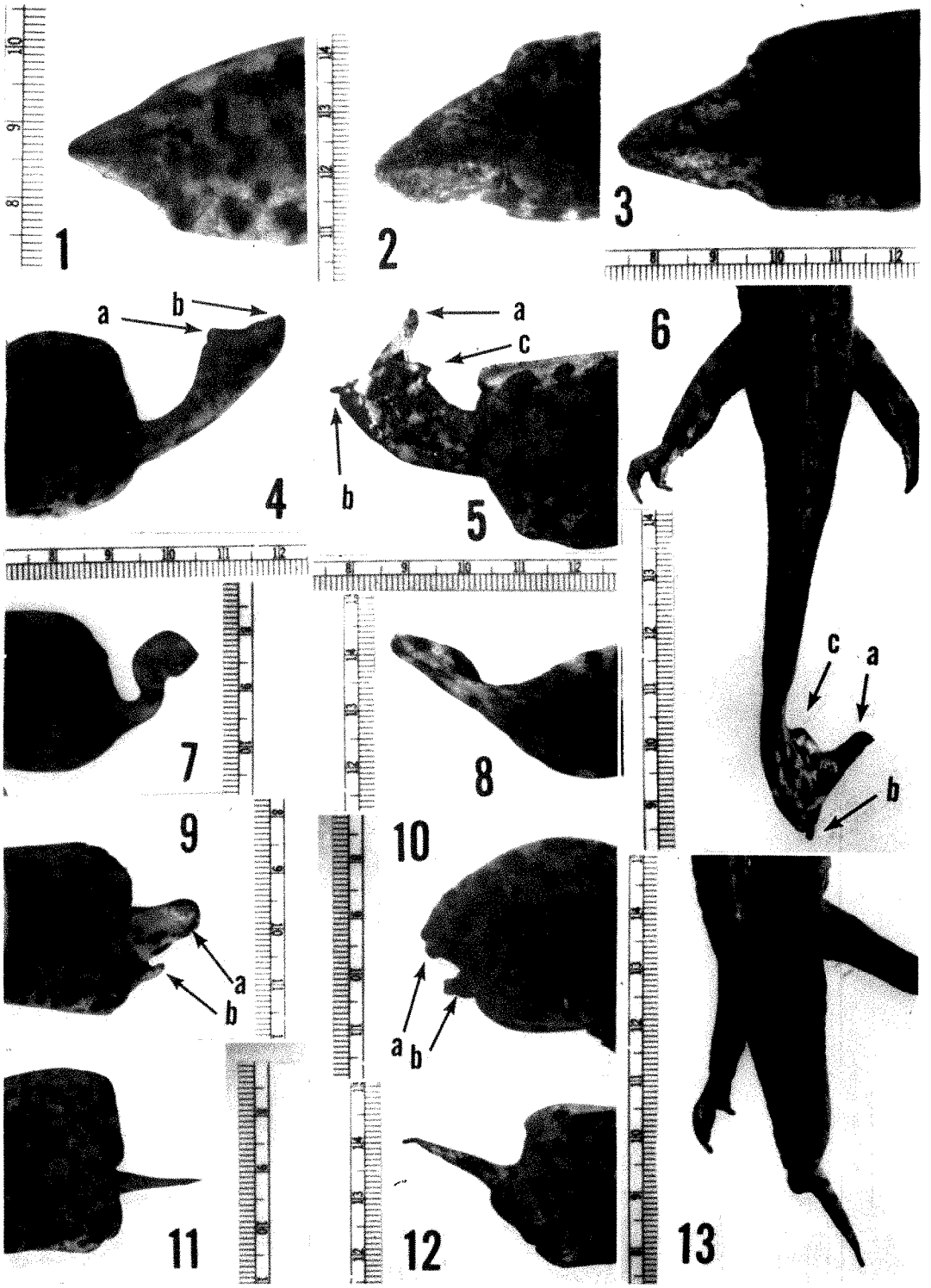
NORMAL REGENERATION OF THE TAILS OF CONTROL ANIMALS

The gradual development of the tail during normal regeneration is shown in Figures 1–3. The tail is already 14 mm. long 26 days after irradiation, but it is most typical for the regenerate to be very wide in the proximal portion; growth of the regenerate occurs from all of the amputation surface (Fig. 1), and hence the proximal width of the regenerate is about 17 mm. The intensity of regeneration is greatest the first month after amputation; the length of the regenerate is 23 mm. after 89 days (Fig. 2), but no more than 25 mm. after 134 days (Fig. 3). Increase in the width of the regenerate, however, is characteristic of this stage of regeneration.

A general picture of the histology of a normal regenerate is provided in Figures 14 and 15. The axial skeleton and the spinal cord are surrounded by a very large region consisting of loose connective tissue, with blood vessels, especially capillaries, but very few muscles. Differentiation of the axial skeleton is highly typical.

A previous study[14] dealt in part with the normal development of the tail of the young axolotl. During the first period (2 or 3 months), development of the axial skeleton of the tail is limited to growth and development of the notochord. The second period begins with the formation of the cartilaginous trunk in the distal portion of the axial skeleton of the tail. The cartilaginous trunk is usually a long and narrow skeletal element without any differentiation during the early stages of development.

In adult tail regenerates fixed 134 days


1
2
3
a
b
4
a
c
b
5
6
c
a
b
7
8
9
a
b
10
a
b
11
12
13

after amputation, rapid differentiation of the cartilaginous trunk, beginning at the actively growing tip, is characteristic. The tip consists of prochondral cells with many mitotic figures (Fig. 17). In the more proximal region (Fig. 16), these prochondral cells are transformed into completely differentiated cartilaginous cells. Four successive zones of the transformation process can be distinguished among the cartilaginous cells (Fig. 16; and 1–4). In the more proximal portions of the cartilaginous trunk, metameric differentiation of cartilaginous tissue, corresponding to the future formation of vertebrae, is highly typical of normal regeneration (Fig. 14; and 15).

In normal regenerates, the spinal cord is characterized by a very monotonous structure in the tail, from the proximal region to the very end. Expansion and duplication of the central canal are never observed in normal regenerates.

The Structures of Monstrous Regenerates Developing from Partially Irradiated Tails

The morphology of the 12 monstrous regenerates exhibited all grades of deviation from normal, ranging from almost normal structures to completely abnormal ones without axial skeleton or spinal cord. Even when similar in outward appearance, some of these regenerates were very different in structure. Furthermore, the cartilaginous trunk did not undergo normal metameric differentiation in any monstrous regenerate in which it developed at all.

The 12 monstrous regenerates can be considered in order of increasing abnormality.

1. A-65-33. A paddle-shaped regenerate (Fig. 4), with the axial skeleton and spinal cord almost normal to the end, without bifurcation. The only abnormality evident, in fact, is absence of normal differentiation of the cartilaginous trunk.

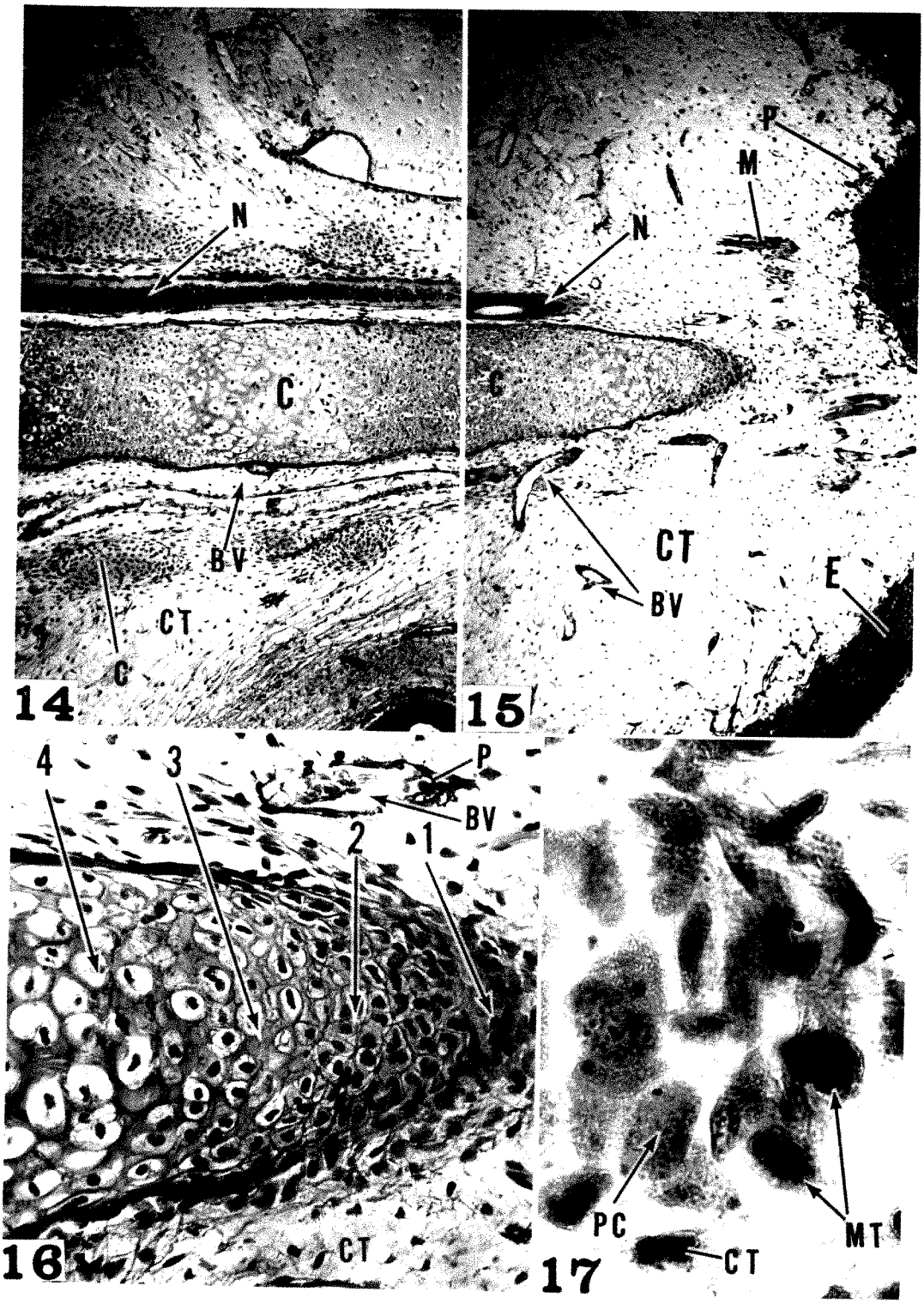
2. D-65-8. A long and narrow regenerate, with the axial skeleton and spinal cord almost normal to the end (Fig. 19).

3. A-65-35. A long, narrow, contorted regenerate (Fig. 7), with the axial skeleton and spinal cord almost normal in the distal portion (Fig. 24), but the cartilaginous trunk abnormally thick in the proximal and middle portions (Fig. 21; and 25).

4. D-65-21. A highly abnormal-looking regenerate, small, awlshaped, round in cross section (Fig. 12; and 13). The axial skeleton and spinal cord, however, are almost normal to the end (Fig. 18).

Plate I.

Fig. 1–3. Normal regenerates of control Animals 26 (1), 89 (2), and 134 (3) days after amputation.
Fig. 4. Regenerate of Animal A-65-33 (No. 1) 420 days after second amputation (539 days after irradiation with 1,000 r). a, b, distal ends of regenerate.
Fig. 5 and 6. Regenerate of Animal D-65-23 (No. 11) 365 days after second amputation (495 days after irradiation with 4,500 r). a, b, c, distal ends of regenerate.
Fig. 7. Regenerate of Animal A-65-35 (No. 3) 410 days after second amputation (539 days after irradiation with 1,000 r).
Fig. 8. Regenerate of Animal D-65-12 (No. 6) 365 days after second amputation (495 days after irradiation with 6,000 r).
Fig. 9. Regenerate of Animal A-65-42 (No. 9) 440 days after second amputation (539 days after irradiation with 2,000 r). a, b, distal ends of regenerate.
Fig. 10. Regenerate of Animal D-65-17 (No. 10) 448 days after second amputation (495 days after irradiation with 4,500 r). a, b, distal ends of regenerate.
Fig. 11. Regenerate of Animal A-65-23 (No. 12) 430 days after second amputation (539 days after irradiation with 2,000 r).
Fig. 12 and 13. Regenerate of Animal D-65-21 (No. 4) 381 days after second amputation (495 days after irradiation with 4,500 r).


N
C
BV
CT
C
14
P
M
N
C
CT
BV
E
15
4
3
P
BV
2
1
CT
16
PC
MT
CT
17

5. D-65-7. A short, wide regenerate, with slight expansion of the cartilaginous trunk and the end of the spinal cord.

6. D-65-12. A long and narrow regenerate (Fig. 8), with considerable expansion of the respective ends of the cartilaginous trunk and the spinal cord.

7. D-65-27. A small and comparatively wide regenerate, with considerable expansion of the respective ends of the cartilaginous trunk and the spinal cord.

8. A-65-36. A small and comparatively wide regenerate, with great expansion of the end of the cartilaginous trunk.

9. A-65-42. A double regenerate, the main regenerate short and comparatively wide and the additional regenerate fairly small (Fig. 9). The regenerate is in the process of reduction. The small regenerate lacks both axial skeleton and spinal cord, and the cartilaginous trunk is completely absent. There is obvious destruction of bony vertebrae by macrophages.

10. D-65-17. A double regenerate, both regenerates very small (Fig. 10). There is expansion of the cartilaginous trunk and the end of the spinal cord. The axial skeleton and the spinal cord do not reach the end of the basal portion of the tail and do not penetrate into either of the regenerates.

11. D-65-23. A comparatively large, paddle-shaped regenerate, with three finger-shaped distal ends (Fig. 5; and 6). The axial skeleton and the spinal cord do not reach the end of the main part of the regenerate and do not penetrate into any of the three ends. There is very great expansion of the end of the cartilaginous trunk, and moderate expansion of the end of the spinal cord.

12. A-65-23. A highly abnormal-looking regenerate, small, awlshaped, round in cross section (Fig. 11), almost identical with No. 4 (D-65-21) in appearance (Fig. 12; and 13), but completely different in structure. The spinal cord and the axial skeleton do not reach the end of the basal portion of the tail and do not penetrate into the regenerate (Fig. 23), which consists only of skin epithelium and loose connective tissue, without any skeleton or spinal cord (Fig. 22).

DISCUSSION

The 12 monstrous regenerates described above represent a wide variety of structures. Even so, one feature is common to all of the monstrous regenerates with axial skeletons, and that is the absence of metameric differentiation of cartilaginous tissue, a process that is highly typical of normal tail regenerates.

Roentgen regression, the destruction of irradiated tissues by macrophages, has been reported a number of times.[1–4,7–11,13–15] Although observed in 90 per cent of regenerates of extremities of adult axolotl during the first 100 to 150 days after irradiation,[10] it was observed in the present study only in one instance.

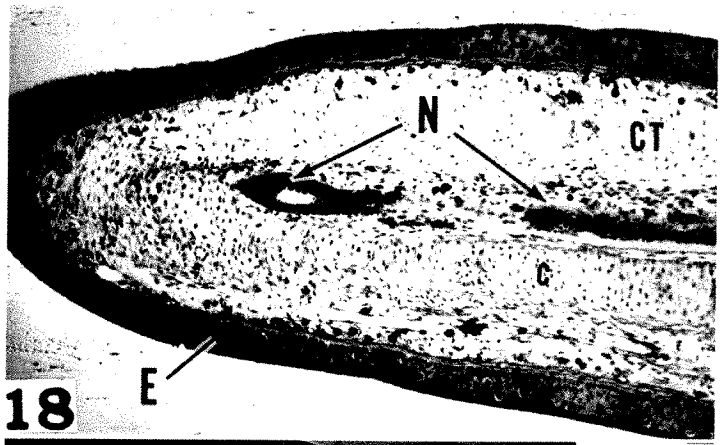
In addition to the absence of normal differentiation of cartilaginous tissue, the monstrous regenerates described in this paper show several general features:

1. A tendency toward being long but narrow. This tendency is manifested in regenerates ranging from large, paddle-

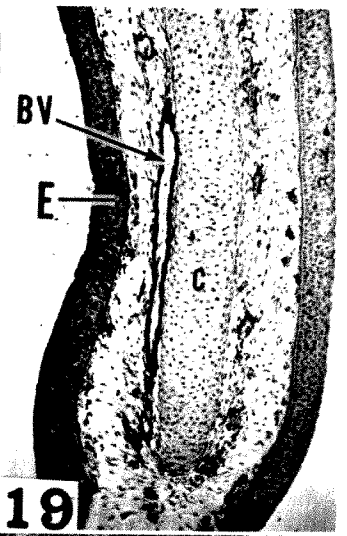
---

PLATE II.

FIG. 14–17. Various sagittal sections through normal regenerate of control animal 134 days after amputation. The proximal portion of the regenerate is shown in Figure 14; distal portions are shown in Figures 15–17. BV, blood vessels; C, cartilaginous trunk or other cartilaginous elements; CT, loose connective tissue (or connective tissue cell); E, skin epithelium; M, muscles; Mt, mitoses; N, spinal cord; P, pigment cells; PC, prochondral cells; 1, 2, 3, 4, stages of differentiation of cartilage in distal portion of cartilaginous trunk. (Fig. 14 and 15, ×42; Fig. 16, ×170; Fig. 17, ×570.)



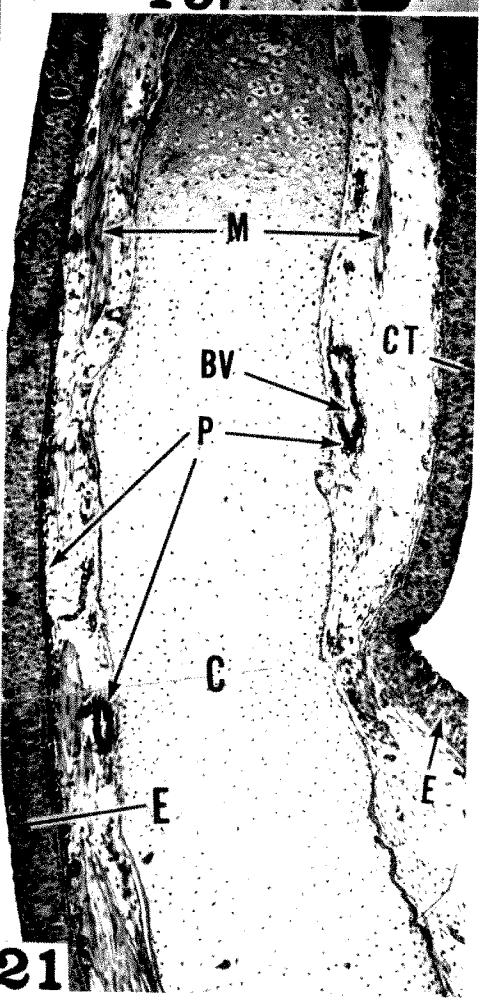
18



19



20



21

shaped ones (Fig. 4; and 5) to small, narrow, awlshaped ones (Fig. 11; and 13). Only in one instance is there no manifestation of this tendency (Fig. 10).

2. A tendency toward forming several distal ends (Fig. 4; 5; 9; and 10). This tendency is evidently not connected with duplication of the axial skeleton and spinal cord—a phenomenon that was never observed in the present study.

3. A tendency toward preserving a comparatively normal structure, even when the appearance is highly abnormal. The extreme case in No. 4 (D-65-21), a small, awlshaped regenerate, with the axial skeleton and the spinal cord almost normal to the end (Fig. 12; and 13).

4. A tendency toward expansion of the axial skeleton and spinal cord, with inhibition of their growth lengthwise, a tendency manifested only in a few cases. Where this tendency is apparent, the end of the cartilaginous trunk is abnormally thick, and does not reach the end of the basal portion of the tail or penetrate into the regenerate.

5. A tendency toward expansion of only the spinal cord, with inhibition of its growth lengthwise, another tendency manifested only in a few cases. This tendency is associated, in some instances, with transformation of the central canal into a large cavity. Bending of the spinal cord and duplication of the central canal may be accompanied by simultaneous immigration of cells into the cavity (Fig. 23). Similar findings were noted after local irradiation of the tails of young axolotls.[2,14]

Two facts are particularly noteworthy: first, despite their great variety in outward appearance, several of the monstrous regenerates are almost normal in structure; and second, despite their tendency toward forming multiple ends, none of the monstrous regenerates exhibit duplication of the axial skeleton and spinal cord. The tendency toward lengthwise growth is the most important stimulus in the regeneration of the amphibian tail. If the regeneration blastema includes enough cells that are undamaged or only slightly damaged, impairment of regeneration is only partial, and the most important portions of the regenerate—the axial skeleton and the cord—are almost normal to the end of the regenerate.

It is not a coincidence that the monstrous regenerates are long and narrow in almost all cases. In a radiation-damaged regeneration blastema, presumably the axial skeleton and the spinal cord are formed first. If no more than a limited number of undamaged or only slightly damaged cells are available, the upper and lower portions of the tail are not formed at all. Only in such a way can the formation of awlshaped regenerates (Fig. 11; and 12) be explained.

If enough undamaged material is available, the axial skeleton and the spinal cord

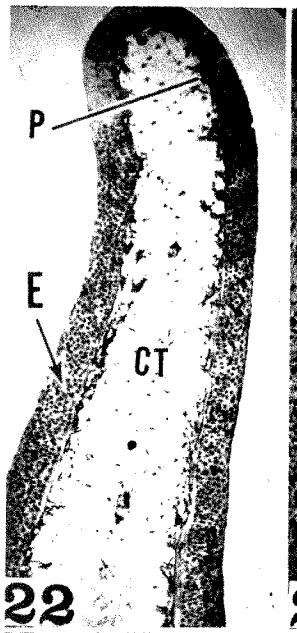
PLATE III.

FIG. 18. Distal portion of regenerate of Animal D-65-21 (No. 4) 381 days after second amputation (495 days after irradiation with 4,500 r). (Same as in Fig. 12 and 13.) C, cartilaginous trunk; CT, loose connective tissue; E, skin epithelium; N, spinal cord. (×42.)

FIG. 19. Distal portion of regenerate of Animal D-65-8 (No. 2) 370 days after second amputation (495 days after irradiation with 6,000 r). BV, blood vessel; C, cartilaginous trunk; E, skin epithelium. (×42.)

FIG. 20. Distal portion of regenerate of Animal D-65-23 (No. 11) 365 days after second amputation (495 days after irradiation with 4,500 r). (Same as in Fig. 5 and 6.) C, abnormal cartilaginous trunk; CT, loose connective tissue; E, skin epithelium; M, muscles; N, distal portion of spinal cord; P, pigment cells. (×42.)

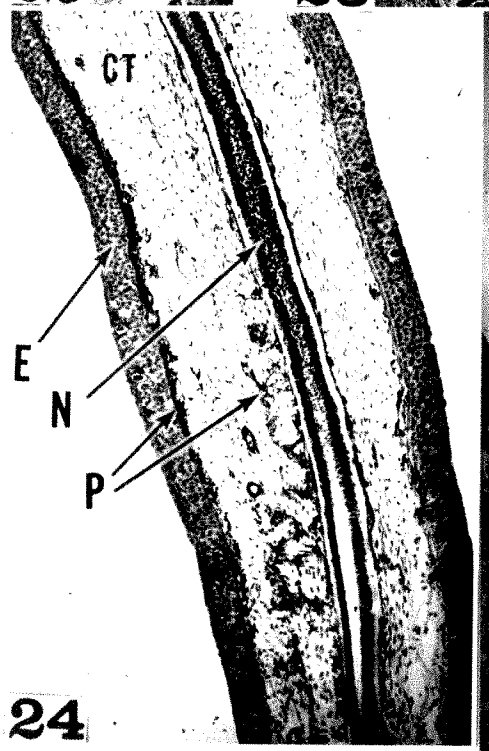
FIG. 21. Middle portion of regenerate of Animal A-65-35 (No. 3) 410 days after second amputation (539 days after irradiation with 1,000 r). (Same as in Fig. 7.) BV, blood vessel; C, abnormal cartilaginous trunk; CT, loose connective tissue; E, skin epithelium; M, muscles; P, pigment cells. (×42.)



22



23



24



25

can obviously be normal and reach the end of the regenerate, as is the case with No. 4 (D-65-21), shown in Figures 12 and 13. If the supply of undamaged material is sufficiently limited, however, the regenerate may consist only of skin epithelium and loose connective tissue and lack any axial skeleton, as is the case with No. 12 (A-65-23), shown in Figure 11. It seems evident that this last case is highly exceptional; even in the absence of enough undamaged material, the regeneration process is very unlikely to involve destruction of the most important parts of the regenerate.

SUMMARY

1. The tails of 115 adult axolotls (*Siredon mexicanum*) were amputated, and the regenerates that developed were irradiated locally 1 to 2 months later with one or another of the following doses: 1,000 r, 2,000 r, 4,500 r, and 6,000 r. A more proximal amputation, performed a relatively long time (more than 1 year) after irradiation, was followed by the development of only 12 regenerates, all monstrous. Obviously these regenerates developed from the boundary zone, where irradiation of the cellular material had been only partial. In the other 103 animals, regeneration was completely suppressed.

2. The 12 monstrous regenerates were the products of limited regeneration, and represented various types of abnormalities, ranging from narrow paddle-shaped formations with almost normal axial skeletons and spinal cords to small and narrow awl-shaped formations lacking both axial skeletons and spinal cords. Regression of the axial skeleton, which has been observed in previous study in 90 per cent of regenerates of axolotl extremities during the first 100 to 150 days after irradiation, was observed in only one instance in the present study. Pathologic changes in the distal portion of the spinal cord were minor and very similar to such changes in irradiated tails of young axolotls, but ingrowth of the spinal cord in the distal portion of the regenerate did not occur in some cases.

The Radiobiology Laboratory
Roswell Park Memorial Institute
Buffalo, New York 14203

REFERENCES

1. Brunst, V. V. Untersuchung des Einflusses von Röntgenstrahlen auf die regenerierenden und erwachsenen Extremitäten bei Urodelen. *Arch. Entwicklungs Mechn. d. Organ*, 1944, *142*, 668–705.
2. Brunst, V. V. Effects of local x-ray irradiation on tail development of young axolotl. *J. Morphol.*, 1950, *86*, 115–151.
3. Brunst, V. V. Influence of local x-ray treatment on development of extremities of young axolotl (Siredon mexicanum). *J. Exper. Zool.*, 1950, *114*, 1–49.
4. Brunst, V. V. Influence of x-rays on limb regeneration in urodele amphibians. *Quart. Rev. Biol.*, 1950, *25*, 1–29.
5. Brunst, V. V. Technics of local low voltage roentgen ray irradiation of experimental animals. *Lab. Invest.*, 1952, *1*, 432–438.
6. Brunst, V. V. Effect of different doses of roent-

Plate IV.

Fig. 22. Distal portion of regenerate of Animal A-65-23 (No. 12) 430 days after second amputation (539 days after irradiation with 2,000 r). (Same as in Fig. 11.) This regenerate has no axial skeleton or spinal cords CT, loose connective tissue; E, skin epithelium; P, pigment cells. (×42.)

Fig. 23. Proximal portion of same regenerate as in Figure 22. Distal portions of axial skeleton (C) and spinal cord (N). (×42.)

Fig. 24. Distal portion of regenerate of Animal A-65-35 (No. 3) 410 days after second amputation (539 days after irradiation with 1,000 r). (Same as in Fig. 7.) CT, loose connective tissue; E, skin epithelium; N, spinal cord; P, pigment cells. (×42.)

Fig. 25. Proximal portion of same regenerate as in Figure 24. BV, blood vessel; C, cartilaginous trunk; CT, loose connective tissue; E, skin epithelium; N, spinal cord. (×42.)

gen rays on adult axolotl (Siredon mexicanum). AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1958, *80*, 126–142.

7. BRUNST, V. V. Roentgen sensitivity of various portions of eye of young axolotl (Siredon mexicanum). AM. J. ROENTGENOL,, RAD. THERAPY & NUCLEAR MED., 1958, *80*, 1014–1030.
8. BRUNST, V. V. Roentgen regression and roentgen stimulation in axolotl (Siredon mexicanum). *Acta Unio internat. contra cancrum*, 1959, *15*, 568–576.
9. BRUNST, V. V. Effect of local x-ray irradiation upon teeth of adult axolotl (Siredon mexicanum). *J. Dent. Res.*, 1959, *38*, 301–310.
10. BRUNST, V. V. Reaction of limb regenerates of adult axolotl (Siredon mexicanum) to x-irradiation. *Radiation Res.*, 1960, *12*, 642–656.
11. BRUNST, V. V. Roentgen regression in axolotl (Siredon mexicanum). AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1961, *85*, 158–178.
12. BRUNST, V. V. New observations concerning roentgen sensitivity of pigment cells in young axolotls (Siredon mexicanum). AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1965, *93*, 222–237.
13. BRUNST, V. V. Effects of ionizing radiation on development of amphibians. *Quart. Rev. Biol.*, 1965, *40*, 1–67.
14. BRUNST, V. V. Histopathology of development of axial skeleton and spinal cord in irradiated tail of young axolotl (Siredon mexicanum). AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1965, *95*, 992–1012.
15. BRUNST, V. V., and SHEREMETEVA, E. A. Sur la perte locale du pouvoir régénérateur chez le triton et l'axolotl causée par l'irradiation avec les rayons X. *Arch. Zool. expér. et génér.*, 1936, *78*, 57–67.
16. BUTLER, E. G. Effects of x-radiation on regeneration of fore limb of amblystoma larvae. *J. Exper. Zool.*, 1933, *65*, 271–315.
17. BUTLER, E. G., and O'BRIEN, J. P. Effects of localized x-radiation on regeneration of urodele limb. *Anat. Rec.*, 1942, *84*, 407–413, 466–467.
18. BUTLER, E. G., and PUCKETT, W. O. Studies on cellular interaction during limb regeneration in amblystoma. *J. Exper. Zool.*, 1940, *84*, 223–237.
19. LITSCHKO, E. J. Observations sur la régénération des extremités des axolotls après l'action des rayons X. *C. R. Acad. Sci. U.S.S.R.*, 1930, *A*, 594–596.
20. LITSCHKO, E. J. Einwirkung der Röntgenstrahlen auf die Regeneration der Extramitäten, des Schwanzes und der Dorsalflosse beim Axolotl. *Trav. Lab. Zool. Exper. Acad. Sci. U.S.S.R.*, 1934, *3*, 101–140.
21. PUCKETT, W. O. Effects of x-radiation on limb development in amblystoma. *Anat. Rec.*, 1934, Suppl. 58, 32–33.
22. PUCKETT, W. O. Effects of x-radiation on limb development and regeneration in amblystoma. *J. Morphol.*, 1936, *59*, 173–213.
23. ROMEIS, B. Mikroskopische Technik. Leibniz Verlag, München, 1948, p. 74.
24. UMANSKI, E. Untersuchung des Regenerationsverganges bei Amphibien. *Biol. Zeitschr.*, 1937, *6*, 739–756.
25. WARREN, S. Histopathology of radiation lesions. *Physiol. Rev.*, 1944, *24*, 225–238.

VOL. 105, NO. 1

THE AMERICAN JOURNAL OF ROENTGENOLOGY RADIUM THERAPY AND NUCLEAR MEDICINE

Editor: TRAIAN LEUCUTIA, M.D.

Assistant to the Editor: KENNETH L. KRABBENHOFT, M.D.

Associate Editors: HARRY HAUSER, M.D., RUSSELL H. MORGAN, M.D., EDWARD B. D. NEUHAUSER, M.D.

Consulting Editorial Board: See front cover.

Published by: CHARLES C THOMAS, Publisher, 301–327 East Lawrence Avenue, Springfield, Illinois 62703.

Issued monthly. Annual subscription: United States, Mexico, Cuba, Central and South America, and Canada $20.00; other countries, $22.00. Current single numbers, $2.00. Advertising rates submitted on application. Editorial office, 401 Professional Building, Detroit, Michigan 48201. Office of publication, 301–327 East Lawrence Avenue, Springfield, Illinois 62703. Information of interest to authors and readers will be found on page ii.

AMERICAN ROENTGEN RAY SOCIETY

President: S. W. Brown, Augusta, Ga.; *President-Elect:* J. C. Cook, Detroit, Mich.; *1st Vice-President:* S. F. Ochsner, New Orleans, La.; *2nd Vice-President:* Herbert M. Stauffer, Philadelphia, Pa.; *Secretary:* T. F. Leigh, Emory University Clinic, Atlanta, Ga. 30322; *Treasurer:* C. B. Holman, Mayo Clinic, Rochester, Minn. 55901.

Executive Council: S. W. Brown, J. C. Cook, S. F. Ochsner, T. F. Leigh, C. B. Holman, T. M. Fullenlove, W. N. Hanafee, J. F. Roach, C. M. Nice, Jr., E. F. Lang, H. O. Peterson, C. A. Stevenson, C. A. Good, T. Leucutia, R. M. Scott, S. W. Nelson, R. L. Tondreau, W. B. Seaman, E. F. Van Epps, Chairman, Duke Univ., Durham, N. C., 27706.

Program Committee: T. F. Leigh, J. F. Roach, T. Leucutia, E. F. Lang, H. O. Peterson, W. N. Hanafee, S. W. Brown, E. F. Van Epps, J. C. Cook, Chairman, LL 14 Professional Plaza, 3790 Woodward Ave., Detroit, Mich. 48201.

Publication Committee: R. H. Greenspan, J. O. Reed, R. N. Cooley, P. A. Riemenschneider, J. F. Roach, Chairman, Albany, N. Y.

Finance and Budget Committee: R. L. Tondreau, W. B. Seaman, G. E. Sheline, J. M. Dennis, T. M. Fullenlove, Chairman, San Francisco, Calif.

Committee on Scientific Exhibits: R. E. Parks, R. G. Lester, W. N. Hanafee, Chairman, UCLA Medical Center, Los Angeles, Calif. 90024.

Advisory Committee on Education and Research: E. C. Klatte, A. R. Margulis, D. M. Witten, F. J. Bonte, C. M. Nice, Jr., Chairman, Dallas, Tex.

Representatives on the American Board of Radiology: J. F. Roach, Albany, N. Y.; S. W. Nelson, Columbus, Ohio; and C. A. Stevenson, Spokane, Wash.

Director of Instruction Courses: H. O. Peterson, Minneapolis, Minn.; *Associate Director:* D. G. Mosser, Minneapolis, Minn.

Manager of the Annual Meeting: E. F. Lang, LL 14 Professional Plaza, 3790 Woodward Ave., Detroit, Mich. 48201.

Editor: T. Leucutia, 401 Professional Building, Detroit, Mich. 48201.

Representative on the Board of Chancellors of the American College of Radiology: S. F. Ochsner.

Seventieth Annual Meeting: Washington-Hilton Hotel, Washington, D. C., September 30–October 3, 1969.

AMERICAN RADIUM SOCIETY

President: Juan A. del Regato, Colorado Springs, Colo.; *President-Elect:* Fernando G. Bloedorn, Boston, Mass.; *1st Vice-President:* Clifford L. Ash, Toronto, Ont., Canada; *2nd Vice-President:* H. Peter Mueller, Boston, Mass.; *Secretary:* John V. Blady, The Parkway House, 2201 Benjamin Franklin Parkway, Philadelphia, Pa. 19130; *Treasurer:* James F. Nolan, 1407 South Hope St., Los Angeles, Calif. 90015.

Executive Committee: Justin J. Stein, Chairman, Los Angeles, Calif.; Juan A. del Regato; Fernando G. Bloedorn; Clifford L. Ash; H. Peter Mueller; John V. Blady; James F. Nolan; Milton Friedman; John L. Pool.

Scientific Program Committee: Juan A. del Regato, Chairman; Fernando G. Bloedorn, Vice-Chairman; Simon Kramer; Wm. E. Powers; Felix N. Rutledge; Jerome M. Vaeth.

Arrangements Committee: Luther W. Brady, Chairman, Philadelphia, Pa.; Gordon Verity, Chairman Designate; Larry McGowan; David Sklaroff; Antolin Raventos; James F. Nolan.

Publication Committee: Harry Hauser, Chairman, Cleveland, Ohio; Giulio J. d'Angio; William T. Moss.

Public Relations Committee: Antolin Raventos, Chairman; Robert Robbins; Harvey P. Groesbeck; Gordon Verity, *ex officio.*

Janeway Lecture Committee: Clifford L. Ash, Chairman, '69, Toronto, Ont., Canada; A. N. Arneson, '71; Milford D. Schulz, '73.

Representatives on the American Board of Radiology: Donald S. Childs, Rochester, Minn.; Justin J. Stein, Los Angeles, Calif.; Ralph M. Scott, Louisville, Ky.

Liaison Representatives on the National Council on Radiation Protection and Measurements: Herbert M. Parker, Richland, Wash.; Marvin M. D. Williams, Rochester, Minn.

Representative on the Board of Chancellors of the American College of Radiology: Charles G. Stetson.

Fifty-first Annual Meeting: Bellevue Stratford Hotel, Philadelphia, Pa., April 28–30, 1969.

EDITORIALS

THE FIFTY-FIRST ANNUAL MEETING OF THE AMERICAN RADIUM SOCIETY

THE 1969 meeting of the American Radium Society will take place at the Bellevue-Stratford Hotel in Philadelphia, April 27th to April 30th, 1969. Over half a century ago, Philadelphia witnessed the birth of the American Radium Society. The eighteen charter members of the Society gathered at the Rittenhouse Hotel for the first Annual Meeting, in 1916; they approved the initial version of the statutes, elected a president, Dr. W. H. B. Aikens, of Toronto, and other officers and members of committees. Dr. D. T. Quigley, of Omaha, is the only surviving member of this group of pioneers who launched the American Radium Society on its venturous course; Dr. J. T. Case, Editor of the Journal, was one of the founders; Dr. H. K. Pancoast was the one Philadelphian among them. Only once, in 1931, did the Society return to the place of its origin. Now that the Society can look proudly on fifty years of valuable contributions, it is only proper that its members return to the historical city that witnessed, also, the birth of the American democracy.

The Scientific Program Committee is presenting the membership with a compact series of papers by national and foreign authorities. A Preliminary Program appears elsewhere in this issue of the JOURNAL. The chosen presentations emphasize the moving trends and activities directed to meet the growing challenge of cancer as a public health problem. The program will be divided in three morning Sessions under the Chairmanship of Drs. F. Bloedorn, President-elect, C. L. Ash, First Vice-President, and P. H. Mueller, Second Vice-President of the Society. The program will feature important contributions by outstanding speakers.

The Janeway Lecture will be delivered by Dr. Franz Buschke, Professor of Radiology and Chief of the Section on Therapeutic Radiology of the University of California Medical Center, San Francisco. Dr. Buschke's chosen subject, "*Radiation Therapy, Past, Present and Future,*" is certain to highlight the Scientific Program. Other eminent speakers are: Dr. Margaret Sloan, Associate Director for Organizational Liaison, Regional Medical Programs; Dr. Gordon Zubrod, Scientific Director for Chemotherapy, National Cancer Institute; and Dr. Laurance V. Foye, Jr., Chief of the Clinical Investigations Branch, Extramural Activities, National Cancer Institute.

Distinguished foreign participants will enrich the Scientific Program with their contributions: Dr. Jean Dutreix and Dr. C. M. Lalanne, of the Institut Gustave Roussy, Villejuif, France, will present important papers on their experiences in the treatment of tumors of the upper passages and with different types of fractionation. Dr. H. J. G. Bloom, of the Royal Marsden Hospital, of London, and Dr. Stanley Dische, of the Mount Vernon Hospital, of Middlesex, England, will also make important contributions to the program, on cancer of the breast and soft tissue sarcomas.

The traditional reception offered by the Radium Chemical Company will highlight the social events; the Atomic Energy of Canada, Ltd. will graciously offer a cocktail party. The Annual Banquet will be the setting in which the Janeway Medal, an

enviable award with a wise message, will be presented to Dr. Franz Buschke; Dr. John L. Pool will also receive a past-President certificate at the banquet. And there will be dancing.

Dr. Luther Brady is Chairman of the Committee of Local Arrangements, composed by Drs. A. Raventos, D. Sklaroff and L. McGowan; they have been at work for some time to make certain that all aspects of the meeting are a success. Mrs. Herbert M. Stauffer, an assurance in herself of charming hospitality, is the Chairman of the Ladies' Committee. The scientific presentations and executive sessions of the Society are scheduled to take place in three mornings, Monday, Tuesday and Wednesday; the afternoons, and the preceding Sunday, are left free for the participants to take advantage of the varied cultural, historical, and sportive opportunities of the city.

There are, in Philadelphia, historical gems a short distance from the Bellevue-Stratford Hotel: registrants and their spouses may wish to visit Carpenter's Hall, Independence Hall, Betsy Ross House or the American Swedish Historical Museum, the Presbyterian Historical Society, the Franklin Institute. Whole day trips, including luncheon and visit to the gardens and colonial rooms of *Winterthur*, will be available to the ladies. Tours of the city, of the Philadelphia Museum of Art and colonial houses in Fairmount Park will also be available. The fabulous *Barnes Foundation* and its rich and varied collection of art will be open to limited members and only on Sunday, April 27th; those interested are asked to write to the Foundation in advance.

Registration to the Annual Meeting will be open to all those interested. Non-members of the Society pay a nominal registration fee. Residents in training who prove their status will be registered free.

The meeting in Philadelphia should be a memorable experience. We hope to see you there!

J. A. del Regato, M.D.

Penrose Cancer Hospital
Colorado Springs, Colorado 80907



ARTHUR C. SINGLETON, M.D.
1900–1968

ARTHUR CARMAN SINGLETON of Toronto, Ontario, was born January 3, 1900 in the eastern Ontario hamlet of Newboro. He entered the University of Toronto in 1917 but left in the spring of 1918 and enlisted as a private in the First Canadian Tank Battalion. He was discharged from the army in 1919 and reentered University, obtaining his medical degree in 1923. He interned in St. Luke's Hospital, Minneapolis, and in 1924 entered training with Dr. Douglas Quick at Memorial Hospital, New York. In 1925 he was appointed to the staff of the Toronto General Hospital, and the University of Toronto. In addition, in 1929 he became associated with Drs. Gordon Richards and Howard Dickson in the private practice of Radiology.

At the outbreak of World War II in 1939, Dr. Singleton became Radiologist to No. 15 General Hospital, Royal Canadian Army Medical Corps, and as Consultant Radiologist to the Canadian Army overseas. He

returned to Canada in 1943 and was appointed Consultant Radiologist of the Royal Canadian Air Force, with the duties of developing and overseeing all air-force radiological installations and radiologist-training programmes. In recognition of his services to his country, Dr. Singleton was awarded the MBE (Member of the British Empire) and the ED (Efficiency Decoration).

At the time of the organization of the Canadian Association of Radiologists in 1937 he became its Honorary Secretary-Treasurer, a post which he held for three years. Since then he served on many Committees of the Association, and in 1948 was elected President. He has been a Vice-President of the Radiological Society of North America and has served the American College of Radiology in several capacities, including membership on the Board of Chancellors and the Judiciary Committee. Dr. Singleton assumed the presidency of the College in 1957, following the death of Dr. Ira Lockwood. In 1951 he was made a Fellow of the Royal College of Physicians and Surgeons of Canada, and in 1960 he was awarded an Honorary Fellowship in the Faculty of Radiologists (London).

Dr. Singleton returned to civilian status in 1945 and since 1950 was Professor and Head of the Department of Radiology at the University of Toronto and Radiologist-in-Chief of the Toronto General Hospital. He was a Consultant Radiologist to Sunnybrook Veterans Hospital, and the Hospital for Sick Children, Toronto. In June 1962 Dr. Singleton retired from these posts and was appointed Professor Emeritus of Radiology. In this year, however, the culmination of the many honours bestowed upon him was brought into being, after serving as President-Elect, by his appointment as President of the Tenth International Congress of Radiology, held in the City of Montreal, Quebec.

Dr. Singleton has made numerous contributions to scientific literature in medical periodicals and textbooks. His prominence as an educator is demonstrated by the fact that about fifteen per cent of Canada's practicing radiologists came at one time or another under his tutelage.

Despite a busy professional life Dr. Singleton managed from time to time to enjoy his hobbies of movie-photography and golf.

Dr. Singleton's achievements speak for his unbounded energy and ability. He will always be remembered by his friends and colleagues for his happy out-going nature. He was always humble, kind and considerate, living by a definite set of principles.

We express our deepest sympathy to his wife, Marion Singleton, and his daughter, Mrs. R. J. Paterson, and to the four grandchildren to whom he was so greatly devoted.

M. R. Hall, M.D.

Department of Radiology
Faculty of Medicine
University of Toronto
101 College Street
Toronto 2, Ontario, Canada

THE AMERICAN RADIUM SOCIETY

FIFTY-FIRST ANNUAL MEETING PRELIMINARY PROGRAM

BELLEVUE-STRATFORD HOTEL, PHILADELPHIA, PENNSYLVANIA
APRIL 27–30TH, 1969

Sunday, April 27, 1969

9:00 A.M.–3:00 P.M.
Executive Committee Meeting
Justin J. Stein, M.D., Chairman

12:00 NOON–6:00 P.M.
Registration, 18th floor

Monday, April 28, 1969

Rose Garden, 18th Floor

8:00 A.M.–4:00 P.M. Registration

8:30 A.M.
Welcome Address.
Theodore H. Mendell, M.D., President, Philadelphia County Medical Society.

8:40 A.M.
Presidential Address.
The Community Cancer Hospital. J. A. del Regato, M.D., Penrose Cancer Hospital, Colorado Springs, Colorado.

FIRST SCIENTIFIC SESSION

Fernando G. Bloedorn, M.D., Chairman. Tufts-New England Medical Center Hospitals, Boston, Mass.

9:00 A.M.–9:15 A.M.
Ten Years' Experience with Supervoltage Radiotherapy of Advanced Carcinoma of the Cervix. C. L. Ash, M.D., and W. E. C. Allt, M.D., Ontario Cancer Institute, Toronto, Canada.

9:15 A.M.–9:30 A.M.
Carcinoma of the Cervix: The Use of an Integrated System of Treatment Using a Linear Intracavitary Irradiation Source and External Irradiation. J. Newall, M.B., St. Vincent's Hospital and Medical Center, New York, N. Y., and B. Sischy, M. B., Highland Hospital, Rochester, N. Y.

9:30 A.M.–9:45 A.M.
Complications in 831 Patients with Squamous Cell Carcinoma of the Intact Uterine Cervix Treated with 3,000 Rads or More Whole Pelvis Irradiation. M. F. Strockbine, J. E. Hancock, and G. H. Fletcher, M. D. Anderson Hospital, Houston, Texas.

9:45 A.M.–10:00 A.M.
Significance of Postoperative Irradiation in Carcinoma of the Cervix; a Ten Year Survey. Ruth Guttmann, M.D., Francis Delafield Hospital, New York, N. Y.

10:00 A.M.–10:15 A.M.
Tumor Regression in Carcinoma of the Uterine Cervix: Prognostic Significance. V. A. Marcial, M.D., A. Bosch, M.D., and R. Marcial-Rojas, M.D., Puerto Rico Nuclear Center, Rio Piedras, Puerto Rico.

10:15 A.M.–10:30 A.M.
Late Second Cancers of the Cervix After Apparently Successful Initial Radiation Therapy. A. Brunschwig, M.D., and J. Barrie, M.D., Memorial Hospital Center, New York, N. Y.

10:30 A.M.–11:00 A.M.
Intermission.
Refreshments served in the Terrace Room.

11:00 A.M.–11:20 A.M.
The Role of the Regional Medical Program in the Care of Cancer Patients. Margaret H. Sloan, M.D., Public Health Service, Department of Health, Education and Welfare, Bethesda, Md.

11:20 A.M.–11:30 A.M.
Temporary Spontaneous Regression of Isologous Tumor Transplants in Irradiated Tissue. H. G. Seydell, M.D., K. Sloan, M.D., and S. Berk, M.D., University of Maryland School of Medicine, Baltimore, Md.

11:30 A.M.–11:40 A.M.
Pre-operative *vs.* Post-operative Irradiation. Experimental Observations on an Animal Tumor System. C. A. Perez, M.D., and J. Olson, R.N., Washington University, St. Louis, Mo.

11:40 A.M.–11:55 A.M.
A Metabolic Control for the Enhancement of Radiation Response. J. E. Biaglow, Ph.D., and Hymer L. Friedell, M.D., Western Reserve University, Cleveland, Ohio.

12:00 NOON–1:00 P.M.
Symposium: Tumors of the Eye
Simon Kramer, M.D., Chairman, Jefferson Hospital, Philadelphia, Pa. George Merriam, M.D., Institute of Ophthalmology, New York, N. Y.; Malcolm Bagshaw, M.D., Stanford Medical Center, Palo Alto, California; Elizabeth Focht, Ph.D., New York Hospital-Cornell Medical Center, New York, N. Y.

1:00 P.M.
Adjournment of the First Scientific Session.

6:30 P.M.
Reception for all Members and Guests, Rose Garden, 18th floor. Host: Radium Chemical Company.

Tuesday, April 29, 1969

7:45 A.M.
Breakfast
First Executive Session for all Members. North Cameo Room, 18th Floor

Second Scientific Session

Rose Garden, 18th Floor
Clifford L. Ash, M.D., Chairman.
Princess Margaret Hospital, Toronto, Canada.

9:00 A.M.–9:15 A.M.
The Natural History and Radiation Therapy of Carcinoma of the Lip—A Study of 550 Cases. J. F. Bohorquez, M.D., Michael Reese Hospital, Chicago, Ill.

9:15 A.M.–9:30 A.M.
Integrated Radical Radiotherapy and Surgery for Intra-Oral and Laryngeal Cancer. B. Roswit, M.D., H. Kolson, M.D., R. Spiro, M.D., and PoYoung Lin, M.D., Veterans Administration Hospital, Bronx, N.Y.

9:30 A.M.–9:45 A.M.
Therapeutic Integration of Cancer of the Larynx: Analysis of 151 Cases. G. Garcia, M.D., V. Acosta, M.D., and I. Algorri, M.D., Hospital Español, México, D.F.

9:45 A.M.–10:00 A.M.
The Place of Radiotherapy in the Management of the Squamous Cell Carcinoma of the Supraglottic Region. G. H. Fletcher, M.D., R. H. Jesse, Jr., M.D., R. D. Lindberg, M.D., and C. R. Koons, M.D., M. D. Anderson Hospital, Houston, Texas.

10:00 A.M.–10:20 A.M.
Telecobalt Therapy for Carcinoma of the Hypopharynx and Larynx. C. M. Lalanne, M.D., Institut Gustave Roussy, Villejuif, France.

10:20 A.M.–10:30 A.M.
Carcinoma of the Vocal Cords: Treatment Failure and Cobalt-60 Dosimetry. B. H. Feder, M.D., V. A. Hospital, Long Beach, Calif., J. W. Schaeflein, M.Sc., V.A. Hospital, Long Beach, Calif., and J. J. Stein, M.D., U.C.L.A. School of Medicine, Los Angeles, Calif.

10:30 A.M.–11:00 A.M.
Intermission.
Refreshments served in the Terrace Room.

11:00 A.M.–11:20 A.M.
Cooperative Clinical Research of the National Cancer Institute. Laurance V. Foye, Jr., M.D., National Institutes of Health, Bethesda, Md.

11:20 A.M.–11:40 A.M.
Regression of Tumors of the Tonsil Following Different Regimes of Fractionation. J. Dutreix, M.D., and A. Wambersie, M.D., Institut Gustave Roussy, Villejuif, France.

11:40 A.M.–11:55 A.M.
Pilot Study of Dose Fractionation in Carcinoma of the Base of the Tongue: Uninterrupted *Versus* Split-Course Irradiation. V. A. Marcial, M.D., and Z. Frias, M.S., Puerto Rico Nuclear Center, Rio Piedras, Puerto Rico.

12:00 NOON–1:00 P.M.
Janeway Lecture: Radiation Therapy, Past, Present and Future. Dr. Franz Buschke, University of California Medical Center, San Francisco, Calif.

1:00 P.M.
Adjournment of the Second Scientific Session.

1:30 P.M.
Luncheon of the American Society of Therapeutic Radiologists. North Cameo Room, 18th floor

7:00 P.M.
Cocktail Party. Host: Atomic Energy of Canada, Ltd. Reception and Annual Banquet—Rose Garden, 18th floor. Presentation of the Janeway Medal. Presentation of past-President Certificate.

Wednesday, April 30, 1969

7:45 A.M.
Breakfast
Second Executive Session for all Members. North Cameo Room, 18th floor

Third Scientific Session

Rose Garden, 18th floor
Peter H. Mueller, M.D., Chairman.
Anna Jacques Hospital, Newburyport, Mass.

9:00 A.M.–9:15 A.M.
Pseudolymphomas: Diagnosis and Treatment. R. Robbins, M.D., and A. R. Peale, M.D., Temple University, Philadelphia, Pa.

9:15 A.M.–9:30 A.M.
Patterns of Progression and Factors Influencing Recurrence of Malignant Lymphomas. D. W. Molander, M.D., and G. Lacayo, M.D., Pack Medical Foundation, New York, N. Y.

9:30 A.M.–9:45 A.M.
Neuroblastoma—A Study of 144 Cases Treated in the Institut Gustave Roussy Over a Period of Seven Years. J. G. Stella, M.D., Jefferson Medical College Hospital, Philadelphia, Pa., O. Schweisguth, M.D., and Michel Schlienger, M.D., Institut Gustave Roussy, Villejuif, France.

9:45 A.M.–10:00 A.M.
Wilms' Tumor: Evolution of a Treatment Program. R. H. Sagerman, M.D., B. Schneider, M.D., J. A. Wolff, M.D., and T. V. Santulli, M.D., Upstate Medical Center, Syracuse, N.Y.

10:00 A.M.–10:15 A.M.
Irradiation of the Liver in Children: Early and Late Effects. M. Tefft, M.D., D. Traggis, M.D., R. Filler, M.D., and G. F. Vawter, M. D., The Children's Hospital Medical Center, Boston, Mass.

10:15 A.M.–10:30 A.M.
Radiation Therapy of Carcinoma of the Penis. Jerome M. Vaeth, M.D., Mount Zion Hospital, Claire Zellerbach Saroni Tumor Institute, San Francisco, Calif.

10:30 A.M.–11:00 A.M.
Intermission.
Refreshments served in the Terrace Room.

11:00 A.M.–11:20 A.M.
Chemotherapy of Malignant Tumors. C. Gordon Zubrod, M.D., National Cancer Institute, Bethesda, Md.

11:20 A.M.–11:40 A.M.
Host Resistance and Survival in Medullary Carcinoma of the Breast. H. J. G. Bloom, M.D., Royal Marsden Hospital, London, England.

11:40 A.M.–12:00 P.M.
Radiotherapy in the Management of Sarcomas of the Soft Tissues. Sir Brian Windeyer, M.D., Middlesex Hospital, London, and S. Dische, M.D., Mount Vernon Hospital, Middlesex, England.

12:00 P.M.–12:15 P.M.
Complete Histories of Patients With Metastatic Cervical Lymph Nodes Successfully Treated More than Five Years Ago with Our Economical Combined Radiation Technic. Charles L. Martin, M.D., The Martin X-Ray and Radium Clinic, Dallas, Texas.

12:15 P.M.–12:30 P.M.
The Management of the Teeth, Bone, and Soft Tissues in Patients Receiving Treatment for Oral Cancer. J. J. Stein, M.D., Los Angeles, Calif., A. G. James, M.D., Columbus, Ohio, and E. R. King, M.D., Richmond, Va.

12:30 P.M.–12:45 P.M.
Moving Strip Irradiation in the Treatment of Extensive Neoplastic Disease in the Chest. C. Botstein, M.D., G. Schwarz, M.D., F. Mincer, M.D., G. Zacharopoulos, M.S., and R. McDougall, B.S., Montefiore Hospital, Bronx, N. Y.

12:45 P.M.–1:00 P.M.
Total Abdominal Cobalt 60 Irradiation by Moving Strip Therapy. A. Friedmann, M.D., D. Benninghoff, M.D., B. Aron, M.D., and L. Alexander, M.D., State Univ. of N.Y., Down State Medical Center, Brooklyn, N. Y.

1:00 P.M.–1:15 P.M.
Third Executive Session for all Members.
Rose Garden, 18th floor
Installation of new officers

1:15 P.M.
Adjournment of the Fifty-first Annual Meeting of the American Radium Society.

INTERNATIONAL COMMISSION ON RADIATION UNITS AND MEASUREMENTS (ICRU)

THE International Commission on Radiation Units and Measurements has just published ICRU Report 11, *Radiation Quantities and Units.*

In the Foreword, Lauriston S. Taylor, Chairman of ICRU states:

ICRU Report 10a entitled *Radiation Quantities and Units* was first published in 1962 by the U. S. National Bureau of Standards on behalf of the Commission. When a reprinting of the initial document became necessary in 1964, small modifications and corrections were incorporated.

Now that a second reprinting is required, additional limited modifications and corrections are incorporated that have been approved by the Commission at its 1967 meeting.

In this document the International System of Units (SI) has been adopted.

Because of the continuing requirements for additional quantities and further clarification of the older quantities, future reports are envisaged. The Commission is presently examining the symbolism to be used in these future reports. It is also considering modifications of the sections on Limiting Procedures and on Spectral Distributions and Mean Values. A study of concepts for radiation protection purposes and incorporation of additional macroscopic and of microscopic concepts are planned.

The scope of the ICRU is defined as follows: The International Commission on Radiation Units and Measurements (ICRU), since its inception in 1925, has had as its principal objective the development of internationally acceptable recommendations regarding:

(1) Quantities and units of radiation and radioactivity,

(2) Procedures suitable for the measurement and application of these quantities in clinical radiology and radiobiology,

(3) Physical data needed in the application of these procedures, the use of which tends to assure uniformity in reporting.

The Commission also considers and makes recommendations in the field of radiation protection. In this connection, its work is carried out in close cooperation with the International Commission on Radiological Protection (ICRP).

The policy, current program, available reports of the ICRU, its relationship with other organizations and operative procedure are described in detail.

The membership of the Commission and its subgroups totals 140 persons drawn from 16 countries, indicating the extent to which ICRU has achieved international breadth of membership within its basic selection requirement of high technical competence of individual participants.

The members of the Commission preparing this report were: Lauriston S. Taylor, Chairman; M. Tubiana, Vice-Chairman; H. O. Wyckoff, Secretary; A. Allisy; J. W. Boag (1965–1966); R. H. Chamberlain; F. P. Cowan; F. Ellis (1965); J. F. Fowler; H. Fränz (1965), F. Gauwerky; J. R. Greening; H. E. Johns (1965–1966); K. Lidén; R. H. Morgan; V. A. Petrov (1965); and H. H. Rossi.

NEWS ITEMS

POSTGRADUATE COURSE ON CONTROVERSIES IN ANGIOGRAPHY

Cleveland Clinic Educational Foundation

The Cleveland Clinic Educational Foundation announces a Postgraduate Course on Controversies in Angiography to be held February 12 and 13, 1969 in the Education Building of the Cleveland Clinic.

The purpose of the Course is to present controversial topics concerning both technical and diagnostic facets of angiography.

Angiography of the central nervous system and the heart will not be included.

The Faculty will consist of invited Speakers and the Staff of the Cleveland Clinic.

Further information may be obtained by writing to Walter J. Zeiter, M.D., Director, The Cleveland Clinic Educational Foundation, 2020 East 93rd Street, Cleveland, Ohio 44106.

THE SECOND INTERNATIONAL CONFERENCE ON MEDICAL PHYSICS

In the March 1968 issue of this JOURNAL an announcement was made of the Second International Conference on Medical Physics, which will be held at the Sheraton-Boston Hotel, Boston, Mass., August 11–15, 1969.

Papers may be presented on any aspect of the application of physics and engineering technology to medicine, including applications in nuclear medicine, radiology, cardiology, anesthesiology, surgery and internal medicine.

The emphasis will be on physical techniques to aid medical diagnosis and therapy, including the uses of nuclear radiations, x-rays, heat, light and sound, the measurement of electrical signals in the body, and associated instrumentation and data handling methods.

Abstracts in English of no more than 250 words should be submitted before February 28, 1969.

A brochure on the Conference, together with registration forms and abstract material, is obtainable from: Mr. W. T. Maloney, Conference Coordinator, Second International Conference on Medical Physics, Six Beacon Street, Suite 620, Boston, Massachusetts 02108.

TRENDS IN SYSTEMS FOR THE RADIOLOGIC EXAMINATION OF THE ALIMENTARY TRACT

Biology Seminar

On March 19 through March 22, 1969 the Department of Radiology of Mount Sinai Hospital, Miami Beach, Florida will sponsor a seminar titled Trends in Systems for Radiologic Examination of the Alimentary Tract.

The Seminar, which will be held in the new ultramodern Sheraton Four Ambassadors Hotel in Miami, will inform Diagnostic Radiologists of the latest advances in techniques for the examination of the alimentary tract. Discussion will include, but not be limited to, radiologic equipment (generators, tables, image intensifiers, television systems, tape recorders spot film devices, etc.); processing and viewing equipment; and radiologic techniques.

The Guest Speakers will include: Erik Boijsen, M.D., Associate Professor in Radiology, University of Lund, Sweden; Gerald D. Dodd, M.D., Professor and Director, Department of Radiology, the University of Texas, M. D. Anderson Hospital, Houston, Texas; John H. Feist, M.D., Chairman, Department of Radiology, University of Pittsburgh, Pittsburgh, Pennsylvania; Arthur K. Finkelstein, M.D., Professor of Radiology, The Graduate Hospital, Philadelphia, Pennsylvania; John R. Hodgson, M.D., Chairman, Section of Diagnostic Radiology, Mayo Clinic, Rochester, Minnesota; John W. Hope, M.D., Professor of Radiology, University of

Pennsylvania, Director, Department of Radiology, The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania; Albert Jutras, M.D., Professor of Radiology, University of Montreal, Hospital Hotel-Dieu, Montreal, Canada; J. W. Laws, M.B., F.R.C.P., F.F., Director, Diagnostic Radiology, King's College Hospital, Denmark Hill, London, England; Alexander R. Margulis, M.D., Professor of Radiology, University of California, San Francisco Medical Center; Director, Department of Radiology, Moffit Hospital, San Francisco, California; Richard Marshak, M.D., Radiologist, 1075 Park Avenue, New York, New York; Roscoe E. Miller, M.D., Professor of Radiology, Indiana University Medical Center, Indianapolis, Indiana; Robert D. Moseley, Jr., M.D., Professor and Chairman of Radiology, The University of Chicago, Chicago, Illinois; Kurt Rossman, Ph.D., Professor and Director, Section of Radiologic Sciences, The University of Chicago, Chicago, Illinois; Richard Schatzki, M.D., Associate Clinical Professor of Radiology, Emeritus, Harvard Medical School, Boston, Massachusetts; Charles E. Shopfner, M.D., Professor of Radiology, The University of Missouri School of Medicine; Director, Department of Radiology, The Children's Mercy Hospital, Kansas City, Missouri; Ernest Sternglass, Ph.D., Department of Radiological Physics, University of Pittsburgh, Pittsburgh, Pennsylvania; Robert E. Wise, M.D., Chairman, Department of Diagnostic Radiology, Lahey Clinic Foundation; Chairman, Department of Radiology, New England Baptist Hospital; Associate Clinical Professor of Radiology, Boston University School of Medicine, Boston, Massachusetts; and Bernard S. Wolf, M.D., Professor and Director of Radiology, Mount Sinai School of Medicine, New York, New York.

For additional information please write to Manuel Viamonte, Jr., M.D., Director, Department of Radiology, Mount Sinai Hospital, Miami Beach, Florida 33140.

INTERNATIONAL SYMPOSIUM ON THE CLINICAL APPLICATIONS OF ISOTOPE CLEARANCE MEASUREMENT OF CEREBRAL BLOOD FLOW

The International Symposium on the Clinical Applications of Isotope Clearance Measurement of Cerebral Blood Flow, will be held April 10–12, 1969.

For further information please contact Dr. med. M. Brock, Neurochirurgische Univ.-Klinik, Langenbeckstrasse 1, 65 Mainz, West Germany.

NATIONAL CONFERENCE ON BREAST CANCER

The National Conference on Breast Cancer sponsored by the American Cancer Society and the Cancer Control Program, United States Public Health Service, will be held at the Shoreham Hotel in Washington, D. C. on Thursday, Friday and Saturday, May 8–10, 1969.

A multidisciplinary review of the breast cancer problem in the United States will be presented including epidemiology, etiology, detection, diagnosis, management and control measures. Disappointing as well as successful approaches in combating the disease will be discussed in an effort to identify possible directions for future progress.

The following program has been arranged: May 8, 1969, Epidemiology, Causation and Pathogenesis; Current Control Measures and Their Effectiveness; May 9, 1969, Changing Concepts in Detection and Diagnosis; Research, Resources and Possible Developments for the Control of Breast Cancer; and May 10, 1969, Management of Operable Cases; Management of Inoperable Cases.

All members of the medical and related professions, and research investigators are invited to attend this Conference. There is no registration fee. Preregistration is requested.

For further information please write to: Roald N. Grant, M.D., National Conference on Breast Cancer, American Cancer Society, 219 East 42nd Street, New York, New York 10017.

POSTGRADUATE COURSE IN NEURORADIOLOGY

Columbia-Presbyterian Medical Center

The Department of Radiology, College of Physicians and Surgeons, Columbia University, announces a Postgraduate Course in Neuroradiology to be held at the Columbia-Presbyterian Medical Center, May 12–16, 1969.

The Course is a comprehensive review of diagnostic neuroradiology and is designed primarily for radiologists, neurologists and neurologic surgeons. Emphasis will be placed on basic information used frequently in neuroradiologic diagnosis, especially angiography. Topics of the Course will also include plain skull film diagnosis, pneumography, myelography, systemic diseases affecting the central nervous system and neuroradiologic approaches to the solution of specific clinical problems.

As a special features of the 1969 course the last day (Friday, May 16th) will be devoted to topics in ophthalmology of neuroradiologic interest. It will be possible for a limited number of physicians to register only for the ophthalmologic neuroradiology symposium.

Inquiries should be addressed to the Program Director, Ernest H. Wood, M.D., Neurological Institute of New York, 710 West 168th Street, New York, New York 10032.

POSTGRADUATE COURSE IN GENITOURINARY RADIOLOGY

This Postgraduate Course in Genitourinary Radiology, which will be held May 12–16, 1969, is organized by the Department of Radiology of the Albert Einstein College of Medicine and its affiliated hospitals under the auspices of the Committee on Continuing Medical Education.

The Course is intended for radiologists, urologists, and other physicians interested in the genitourinary system. Attention will be directed toward the practical aspects of specialized diagnostic procedures as well as to a comprehensive review of the present day concepts of genitourinary radiology.

Film interpretation panels will emphasize the approach to diagnostic problems.

The Program Chairman is Milton Elkin, M.D., Professor and Chairman, Department of Radiology, Albert Einstein College of Medicine. The Chairman of Committee on Continuing Medical Education is Harold G. Jacobson, M.D., Professor of Radiology, Albert Einstein College of Medicine and Chief, Division of Diagnostic Radiology, Montefiore Hospital and Medical Center.

A distinguished Guest Faculty will assist the Local Faculty.

The place where the Course will be held is Robbins Auditorium, Albert Einstein College of Medicine, Morris Park Avenue and Eastchester Road, Bronx, New York.

Registration in advance is advised.

SYMPOSIUM ON NEUTRONS IN RADIOBIOLOGY

A Symposium on Neutrons in Radiobiology will be presented November 11–14, 1969, at the Oak Ridge Playhouse in Oak Ridge, Tennessee. The University of Tennessee-Atomic Energy Commission Agricultural Research Laboratory and the Oak Ridge National Laboratory's Health Physics Division will be co-sponsors of the Symposium. Attendance will be limited to 175 to permit extensive and advanced discussions of recent developments.

Following is a partial list of major topics to be discussed in nonconcurrent sessions: Dosimetry, Relative Biological Effectiveness, Repair and Recovery, Genetic Effects, and Modifying Factors. The symposium will emphasize research requirements as well as the current status of research in the subject area. However, there will be at least one review presentation by an individual who is prominent among researchers within the field of each major topic. Hopefully these review presentations will outline past and current research and will serve to provoke and to challenge researchers.

All speakers will be invited. Abstracts of 200 to 400 words in length should be submitted by June 15, 1969. Physics abstracts should be submitted to J. A. Auxier, Oak

Ridge National Laboratory, P. O. Box X, Oak Ridge, Tennessee 37830. Biological abstracts should be submitted to M. J. Constantin, UT-AEC Agricultural Research Laboratory, 1299 Bethel Valley Road, Oak Ridge, Tennessee 37830. A program and a pamphlet containing all the abstracts and a listing of papers to be presented will be sent to each speaker and attendee by about October 1, 1969.

All speakers and attendees are required to preregister. A check in the amount of $20.00, payable to the Symposium on Neutrons in Radiobiology, should be mailed to J. A. Auxier by August 1, 1969.

Proceedings of the symposium will be published promptly after the symposium by a photo-offset process.

The Program Committee members are: J. A. Auxier, Co-Chairman, Oak Ridge National Laboratory; M. J. Constantin, Co-Chairman, UT-AEC Agricultural Research Laboratory; R. L. Murphree, UT-AEC Agricultural Research Laboratory; H. H. Smith, Brookhaven National Laboratory; H. Vogel, University of Tennessee Medical School; and F. S. Williamson, Argonne National Laboratory.

IX SYMPOSIUM NEURORADIOLOGICUM GÖTEBORG

The Ninth Symposium Neuroradiologicum, will be held in Göteborg, Sweden, from August 24 to August 29, 1970.

The Symposium will mainly deal with the following subjects:

1. Hydrocephalus, brain atrophy and cerebral spinal fluid circulation.
2. The central nervous system in the perinatal period. Normal anatomy and developmental disturbances.
3. Advances in ultrasound and diagnostic isotope methods.
4. Cerebral angiography—physiologic and anatomic aspects.
5. Radiobiology of the nervous system.
6. The use of the proton beam in therapy of the brain.

Papers dealing with other subjects may also be accepted.

A scientific as well as a technical exhibition will be arranged in close connection with the scientific meeting.

Further information may be obtained from Ingmar Wickbom, M.D., President, Sahlgren's Hospital, Göteborg, Sweden.

BOOK REVIEW

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

RADIOGRAPHIC POSITIONING AND RELATED ANATOMY. By Isadore Meschan, M.A., M.D., Professor and Director of the Department of Radiology, The Bowman Gray School of Medicine of Wake Forest University, Winston-Salem, N. C.; Consultant in Radiology, Department of Radiology, Walter Reed Army Hospital, Washington, D. C., with the assistance of R. M. F. Farrer-Meschan, M.B., B.S. (Australia), M.D., Research Associate, Department of Radiology, The Bowman Gray School of Medicine of Wake Forest University, Winston-Salem, N. C. Cloth. Pp. 388, with many illustrations. Price, $13.50. Canadian price, $14.60. W. B. Saunders Company, West Washington Square, Philadelphia, Pa. 19105, 1968.

As a companion volume to "An Atlas of Normal Radiographic Anatomy," by the same authors, this text offers a simpler version of radiographic positioning for quick reference. Basic principles of radiography and radiation protection are discussed, with line drawings and sketches included.

Anatomic illustrations and sketches of patient positioning accompany roentgenograms showing standard positions currently in use. A short text discusses each position and describes the placing of the patient.

The authors have divided the human body into 9 areas, describing each examination pertaining to that area. The tenth chapter in the book fulfills the need for descriptions of specialized examinations which have become somewhat routine in the larger X-Ray Departments. Also, for quick reference, the authors have included a glossary and bibliography.

The size of this book adds to its easy use: 7¼ inches by 10½ inches wide, end opening, permitting the user to see the full page with ease. The use of this book will add much to the understanding of anatomy and the standard positions in radiography.

NICHOLAS I. SCOTT

BOOKS RECEIVED

THE HEAD AND NECK—An Atlas of Tumor Radiology. By Gilbert H. Fletcher, M.D., and Bao-Shan Jing, M.D., in collaboration with Max L. M. Boone, M.D., Thomas S. Harle, M.D., and Howard W. Higholt, M.D., Departments of Radiotherapy and Diagnostic Radiology, The University of Texas M. D. Anderson Hospital and Tumor Institute at Houston, Houston, Texas. Cloth. Pp. 380, with many illustrations. Price $20.00. Year Book Medical Publishers, Inc., 35 E. Wacker Drive, Chicago, Ill. 60601, 1968.

PROCEEDINGS OF THE RUDOLF VIRCHOW MEDICAL SOCIETY IN THE CITY OF NEW YORK: Supplement to Volume 26; Published in Honor of Leo M. Davidoff, M.D. Edited by Mark Rayport, M.D., C.M.; Editorial Committee, Joseph Ransohoff II, M.D., and Harry M. Zimmerman, M.D. Cloth. Pp. 444, with some illustrations. Ferdinand Berger & Söhne, Horn, N. O., Austria, 1968.

STATUS OF RESEARCH IN DIAGNOSTIC RADIOLOGY. A report by the Radiology Training Committee of the National Institute of General Medical Sciences, National Institutes of Health, 1967. Paper. Pp. 142. National Institute of General Medical Sciences, National Institutes of Health, Bethesda, Md., 1968.

THE HUMAN BRONCHIAL CIRCULATION IN HEALTH AND DISEASE. Leon Cudkowicz, M.D., M.R.C.P., F.A.C.P., Director, Cardio-Pulmonary Laboratory, Dalhousie University Faculty of Medicine, Halifax, Nova Scotia, Canada. Cloth. Pp. 424, with some illustrations. Price, $18.00. The Williams & Wilkins Company, 428 E. Preston St., Baltimore, Md. 21202, 1968.

LYMPHOGRAPHY OF THE CERVICAL LYMPHATIC SYSTEM. By U. Fisch, Zurich. Cloth. Pp. 179, with many illustrations. Price, $15.00. Canadian price, $16.00. W. B. Saunders Company, West Washington Square, Philadelphia, Pa., 1968.

ADVANCES IN DYNAMIC RADIOACTIVE SCANNING. Compiled and edited by Yen Wang, M.D., D.Sc. (MED.), Associate Professor of Radiology, University of Pittsburgh and Chairman, Department of Radiology, Homestead Hospital, Pittsburgh, Pa. Cloth. Pp. 130, with many illustrations. Price, $8.50. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill. 62703, 1968.

THE PHYSICS OF MEDICAL RADIOGRAPHY. By Arthur Ridgway, and Walter Thumm, British Columbia Institute of Technology, North Vancouver, British Columbia, Canada. Cloth. Pp. 494, with 314 illustrations. Price, $12.50. Addison-Wesley Publishing Company, Inc., Reading, Mass. 01867, 1968.

SPONDYLITIS ANKYLOPOETICA—DIE BECHTEREWSCHE KRANKHEIT. By Wolfgang Dihlmann, Aachen. Cloth. Pp. 106, with many illustrations. Price, DM 49.60. Georg Thieme Verlag, Stuttgart. In the U. S. A. and Canada, Intercontinental Medical Book Corporation, New York, N. Y. 10016, 1968.

PATHOLOGIE MÉDICALE DE LA HANCHE CHEZ L'ADULTE. By Henri Serre, Professeur de Clinique Rhumatologique à la Faculté de Médecine de Montpellier; and Lucien Simon, Professeur à la Faculté de Médecine de Montpellier, Médecin des Hôpitaux. Cloth. Pp. 624, with 328 figures. Price, 150 F. Masson et Cie, Éditeurs, 120 Boulevard Saint-Germain, Paris, France, 1968.

SOCIETY PROCEEDINGS

MEETINGS OF RADIOLOGICAL SOCIETIES*

UNITED STATES OF AMERICA

AMERICAN ROENTGEN RAY SOCIETY
Secretary, Dr. Ted F. Leigh, Emory University Clinic, Atlanta, Ga. 30322. Annual Meeting: Washington-Hilton Hotel, Washington, D.C., September 30–October 3, 1969.

AMERICAN RADIUM SOCIETY
Secretary, Dr. John V. Blady, The Parkway House, 2201 Benjamin Franklin Parkway, Philadelphia, Pa. 19130. Annual meeting: Bellevue Stratford Hotel, Philadelphia, Pa., April, 28–30, 1969.

RADIOLOGICAL SOCIETY OF NORTH AMERICA
Secretary-Treasurer, Dr. Maurice Doyle Frazer, 1744 South Fifty-eighth St., Lincoln, Neb. Annual meeting: Palmer House, Chicago, Ill., Dec. 1–6, 1968.

AMERICAN COLLEGE OF RADIOLOGY
Executive Director, William C. Stronach, 20 N. Wacker Drive, Chicago 6, Ill. Annual meeting: Regency Hyatt House, Atlanta, Ga., Feb. 18–22, 1969.

SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION
Secretary, Dr. Kenneth L. Krabbenhoft, Harper Hospital, Detroit, Mich. 48201. Annual meeting: New York, N. Y., July 13–17, 1969.

AMERICAN BOARD OF RADIOLOGY
Secretary, Dr. C. Allen Good. Correspondence should be directed to Kahler Center Building, Rochester, Minn. 55901.

The oral examinations will be held at the Pittsburgh Hilton Hotel, Pittsburgh, Pa., June 2–6, inclusive, 1969; and at the Statler Hilton Hotel, Dallas, Texas, Dec. 8–12, inclusive, 1969.

The written examination will be held in selected sites, Saturday, June 21, 1969.

The deadline for filing applications for any of the above three examinations was December 31, 1968.

AMERICAN ASSOCIATION OF PHYSICISTS IN MEDICINE
Secretary, Leonard Stanton, Hahnemann Medical College, 230 N. Broad St., Philadelphia, Pa. 19102.

AMERICAN SOCIETY OF THERAPEUTIC RADIOLOGISTS
Secretary, Dr. J. A. del Regato, Penrose Cancer Hospital, Colorado Springs, Colo. 80907.

AMERICAN SOCIETY FOR DIAGNOSTIC ULTRASOUND
Secretary, Dr. Charles C. Grossman, 552 N. Neville St., Pittsburgh, Pa. 15213.

AMERICAN SOCIETY OF NEURORADIOLOGY
Secretary-Treasurer, Dr. Alan E. Zimmer, Danbury, Conn. 06810.

TWELFTH INTERNATIONAL CONGRESS OF RADIOLOGY
President, Dr. Kempo Tsukamoto, 9-1, 4-chome, Angewa, Chiba, Japan. Meeting: Hotel New Otani, Tokyo, Japan, Oct. 6–11, 1969.

TENTH INTER-AMERICAN CONGRESS OF RADIOLOGY
Counselor for the United States, Dr. Juan A. del Regato, Penrose Cancer Hospital, 2215 North Cascade Ave., Colorado Springs, Colo. 80907.
President, Dr. Juan A. del Regato, Colorado Springs, Colo., USA.
Secretary, Dr. F. Bloedorn, Boston, Mass., USA.
Meeting: San Juan, Puerto Rico, 1971.

INTER-AMERICAN COLLEGE OF RADIOLOGY
President, Dr. Oscar Soto, H. Urteaga 480, Lima, Perú.

ALABAMA RADIOLOGICAL SOCIETY
Secretary, Dr. Walter Brower, Birmingham, Ala. Meets time and place of Alabama State Medical Association.

ALASKA RADIOLOGICAL SOCIETY
Secretary, Dr. Bruce C. Wright, Providence Hospital, Anchorage, Alaska. Meets third Wednesday each month.

ARIZONA RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Robert E. Steyskal, 550 W. Thomas Rd., Phoenix, Ariz. 85013. Two regular meetings a year. Annual meeting at time and place of State Medical Association and interim meeting six months later.

ARKANSAS CHAPTER OF AMERICAN COLLEGE OF RADIOLOGY
Secretary-Treasurer, Dr. Wilma C. Diner, Univ. of Arkansas Medical Center, Little Rock, Ark. 72201.

ARKANSAS RADIOLOGICAL SOCIETY
Secretary, Dr. Charles W. Anderson, 1108½ Poplar, Pine Bluff, Ark. Meets every three months and also at time and place of State Medical Association.

ASSOCIATION OF UNIVERSITY RADIOLOGISTS
Secretary-Treasurer, Dr. Alexander Gottschalk, University of Chicago Medical School, Chicago, Ill. 60637. Annual Meeting: University of California, San Francisco, May 7–10, 1969.

ATLANTA RADIOLOGICAL SOCIETY
Secretary, Dr. Donald R. Rooney, Burnt Hickory Road, Marietta, Ga. Meets monthly except during three summer months, on third Tuesday, at the Academy of Medicine, Atlanta, Ga., at 8:00 P.M.

BAVARIAN-AMERICAN RADIOLOGIC SOCIETY
Advisor, Colonel Paul E. Sieber. *Secretary*, Major Peter B. Riesz, USAH Bad Cannstatt, APO 09154, New York. N. Y. Meets quarterly.

BLOCKLEY RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. R. John Gould, 41 Lombardy Rd., Drexel Hill, Pa. 19026.

BLUEGRASS RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Joe Bernard, Central Baptist Hosp., Lexington, Kentucky 40503. Meets quarterly.

BROOKLYN RADIOLOGICAL SOCIETY
Secretary, Dr. Coleman H. Rosenberg, 81–10 Chevy Chase St., Jamaica, N.Y. 11432. Meets first Thursday of each month, October through June.

BUFFALO RADIOLOGICAL SOCIETY
Secretary, Dr. Courtland Van Deusen, 817 Main St., Niagara Falls N. Y. 14301. Meets second Monday evening each month, October to May inclusive., at University Club.

CALIFORNIA RADIOLOGICAL SOCIETY
Secretary-Treasurer: Dr. Leroy K. Mills, 3157 Oakcliff Circle, Carmichel, Calif. 95608. Meets annually during meeting of California Medical Association.

CATAWBA VALLEY RADIOLOGICAL SOCIETY
Secretary, Dr. Emmett R. White, P. O. Box 303, Rutherford College, N. C. 28671. Meets every Friday, Dept. of Radiology, Valdese General Hosp., Valdese, N. C., at 12:00 NOON.

CENTRAL NEW YORK RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. George, Mitchell, Radiology Department, Syracuse Memorial Hospital, Syracuse, N. Y. 13210. Meets first Monday each month, October through May.

CENTRAL OHIO RADIOLOGICAL SOCIETY
Secretary, Dr. Ollie E. Southard, 2787 Tudor Rd., Columbus, O. 43209. Meets second Thursday in October, November, January, and March 15 and May 19 at Fort Hayes Hotel, Columbus, Ohio.

*** Secretaries of societies are requested to send timely information promptly to the Editor.**

Chicago Roentgen Society
Secretary-Treasurer, Dr. Howard C. Burkhead, 2650 Ridge Ave., Evanston, Ill. 60202. Meets third Wednesday of each month, October to April, except December, at the University Club of Chicago.

Cleveland Radiological Society
Secretary-Treasurer, Dr. James Farmer, 18869 Canyon Rd. Fairview Park, Ohio 44126. Meetings at 7:00 P.M. on fourth Monday of October, November, January, February, March and April.

Colorado Radiological Society
Secretary, Dr. Charles E. Seibert, Department of Radiology, Swedish Hospital, 501 E. Hampton, Englewood, Colo. 80110. Meets third Friday of each month at Denver Athletic Club from September through May.

Connecticut Valley Radiologic Society
Secretary, Dr. William W. Walthall, Jr., 130 Maple St., Springfield, Mass. Meets in April and October.

Dallas-Fort Worth Radiological Society
Secretary-Treasurer, Dr. Robert J. Atcheson, 1401 S. Main St., Fort Worth, Texas 76104. Meets monthly, third Monday, at Southwest International Airport at 6:30 P.M.

Detroit Roentgen Ray Society
Secretary, Dr. David P. Corbett, Harper Hospital, Detroit, Mich. 48201. Meets monthly, first Thursday, October through May, at David Whitney House, 1010 Antietam, at 6:30 P.M.

East Bay Radiological Society
Secretary, Dr. Allen B. Freitag, 411 30th Str., Oakland, Calif. 94609. Meets first Thursday each month, Oct. through May, at University Club, Oakland, Calif.

East Tennessee Radiological Society
Secretary-Treasurer, Dr. T. F. Haase, Jr., 205 Medical Arts Building, Knoxville, Tenn. Meets in January and September.

Florida Radiological Society
Secretary, Dr. Robert H. Nickau, Good Samaritan Hospital, West Palm Beach, Fla. 33402. Meets twice annually, in the spring with the annual State Society Meeting and in the fall.

Florida West Coast Radiological Society
Secretary-Treasurer, Dr. Allen L. Sheer, University Community Hospital, 13505 N. 31st St., Tampa, Fla. 33612. Meets in January, March, May, July, September and November.

Georgia Radiological Society
Chapter of the American College of Radiology
Secretary, Dr. Walker Harris, The Medical Center, Columbus, Georgia 31902. Meets in spring and fall at Annual State Society Meeting.

Greater Cincinnati Radiological Society
Secretary-Treasurer, Dr. Owen L. Brown, 2421 Auburn Ave., Cincinnati, Ohio 45219.

Greater Louisville Radiological Society
Secretary-Treasurer, Dr. L. D. LeNeave, 315 E. Broadway, Louisville, Ky. 40202. Meets monthly.

Greater Miami Radiological Society
Secretary-Treasurer, Dr. Sylvan H. Sarasohn, North Miami General Hospital, 1701 Northeast 127th St., North Miami, Fla. 33161. Meets monthly, third Wednesday at 8:00 P.M. at Jackson Memorial Hospital, Miami, Fla.

Greater St. Louis Society of Radiologists
Secretary-Treasurer, Dr. Roland P. Ernst, 3720 Washington Ave., St. Louis, Mo. 63108.

Hawaii Radiological Society
Secretary-Treasurer, Dr. Thomas C. Brown, 1697 Ala Moana Blvd., Honolulu, Hawaii 96815. Meets third Monday of each month at 7:30 P.M.

Health Physics Society
Secretary, R. J. Augustine, National Center for Radiologic Health, 1901 Chapman Ave., Rockville Md. 20852.

Houston Radiological Society
Secretary, Dr. Thomas S. Harle, 1200 Moursond Drive, Houston, Tex. 77025. Meets fourth Monday of each month, except June, July, August and December, at the Doctors' Club, 8:00 P.M., Houston, Tex.

Idaho State Radiological Society
Secretary, Dr. George H. Harris, Bannock Memorial Hospital, Pocatello, Idaho. Meets in the spring and fall.

Illinois Radiological Society, Inc.
Secretary, Dr. C. R. Markivee, 674 North Seminary St., Galesburg, Ill. 61401. Meets in the spring and fall.

Indiana Roentgen Society, Inc.
Secretary, Dr. Edwin F. Koch, Jr., 915 University Ave., Muncie, Ind. 47303. Meets first Sunday in May and during fall meeting of Indiana State Medical Association.

Iowa Radiological Society
Secretary-Treasurer, Dr. J. H. Lohnes, 1948 First Ave., N.E., Cedar Rapids, Iowa 52402. Luncheon and business meeting during annual session of Iowa State Medical Society. The scientific section is held in the autumn.

Kansas Radiological Society
Secretary-Treasurer, Dr. Robert C. Lawson, 310 Medical Arts Bldg., 10th and Horne, Topeka, Kan. Meets in spring with State Medical Society and in winter on call.

Kentucky Chapter, American College of Radiology
Secretary-Treasurer, Dr. Ralph C. Quillin, 1221 S. Broadway, Lexington, Ky. 40504. Meets in April and September.

Kings County Radiological Society
Secretary, Dr. Sidney Hendler, 1880 Ocean Ave., Brooklyn 30, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

Knoxville Radiological Society
Secretary, Dr. Clifford L. Walton, Blount Professional Bldg., Knoxville 20, Tenn. Meetings are held the third Monday of every other month at the University of Tennessee Memorial Research Center and Hospital.

Long Island Radiological Society
Secretary, Dr. Robert J. Hochstim, 1200 Stewart Ave., Garden City, N. Y. 11533. Meets monthly.

Los Angeles Radiological Society
Secretary, Dr. John L. Gwinn, Childrens Hospital of Los Angeles, 4650 Sunset Blvd., Los Angeles, Calif. 90027. Meets second Wednesday of month in September, November, January, April and June at Los Angeles County Medical Association Building, Los Angeles, Calif.

Louisiana-Texas Gulf Coast Radiological Society
Secretary-Treasurer, Dr. Edward A. Sheldon, 109 Doctors Bldg., Beaumont, Texas 77701.

Maine Radiological Society
Secretary-Treasurer, Dr. Robert A. Bearor, Maine Medical Center, Portland, Maine 04102. Meets in June, September, December and April.

Maryland Radiological Society
Secretary, Dr. Henry Startzman, Medical Arts Building. Baltimore, Md.

Massachusetts Radiological Society
Secretary, Dr. Jerome H. Shapiro, Department of Radiology, Boston City Hospital, 818 Harrison Ave., Boston, Mass. 02118.

Memphis Roentgen Society
Secretary-Treasurer, Dr. Webster Riggs, Jr., The University of Tennessee College of Medicine, Department of Radiology, Walter F. Chandler Bldg., 865 Jefferson Ave., Memphis, Tenn. 38103. Meets first Monday of each month at John Gaston Hospital.

Miami Valley Radiological Society
Secretary, Dr. Darwood B. Hance, Reid Memorial Hospital, Richmond, Indiana. Meets third Thursday of fall, winter and spring months at 7:30 P.M. at Miami Valley Hospital, Dayton, Ohio.

Mid-Hudson Radiological Society
Secretary-Treasurer, Dr. Herbert S. Berlin, Hopewell Junction, N. Y. Meets 7:00 P.M., first Wednesday of each month, September to May.

MILWAUKEE ROENTGEN RAY SOCIETY
Secretary-Treasurer, Dr. James E. Bell, 8700 W. Wisconsin Ave., Milwaukee, Wis. 53213. Meets monthly on fourth Monday, October through May, at University Club.

MINNESOTA RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Warren L. Kump, 4243 Glenwood Ave., Minneapolis, Minn. 55422. Meets twice annually, fall and winter.

MISSISSIPPI RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Dan T. Keel, Jr., 504 Chippewa St., Brookhaven, Miss. Meets third Thursday of each month at the Heidelberg Hotel, Jackson, at 6:00 P.M.

MISSOURI RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Arthur A. Porporis, 100 N. Euclid Ave., St. Louis, Mo. 63108.

MONTANA RADIOLOGICAL SOCIETY
Secretary, Dr. Clark Grimm, Great Falls, Montana. Meets at least once a year.

NEBRASKA STATE RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Otto A. Troester, 924 Sharp Building, Lincoln, Nebraska 60508. Meets third Wednesday of each month at 6 P.M. in Omaha or Lincol

NEVADA RADIOLOGICAL SOCIETY
Secretary, Dr. William G. Arbonies, Department of Radiology, St. Mary's Hospital, Reno, Nev.

NEW ENGLAND ROENTGEN RAY SOCIETY
Secretary, Dr. Morris Simon, 330 Brookline Ave., Boston, Mass. 02115. Meets third Friday of each month, October through May, at The Longwood Towers, 20 Chapel Street, Brookline, Mass., at 4:30 P.M. The Annual Meeting will be held May 24 and 25, 1969, at the Hotel Belmont, West Harwich by-the-sea, Cape Cod, Mass. The guest speaker, Dr. Lucy Frank Squire, will present the Twenty-fifth George W. Holmes Lecture.

NEW HAMPSHIRE ROENTGEN RAY SOCIETY
Secretary, Dr. Paul Y. Hasserjian, 1470 Elm St., Manchester, N. H. Meets four to six times yearly.

NEW MEXICO ASSOCIATION OF RADIOLOGISTS
Secretary-Treasurer, Dr. Justin J. Wolfson, Department of Radiology, Bernalillo County-Indian Hospital, Albuquerque, New Mexico.

NEW MEXICO SOCIETY OF RADIOLOGISTS
Secretary, Dr. Phil Fox, Albuquerque, New Mexico. Four meetings annually, three held in Albuquerque, N. M., and one held at time and place of New Mexico State Medical Society annual meeting.

NEW YORK ROENTGEN SOCIETY
Secretary-Treasurer, Dr. Samuel H. Madell, 1 E. 82nd St New York, N. Y. 10024. Meets monthly on third Monday at the New York Academy of Medicine at 4:30 P.M.

NEW YORK STATE CHAPTER OF THE AMERICAN COLLEGE OF RADIOLOGY, INC.
Secretary-Treasurer, Dr. John W. Colgan, 273 Hollywood Ave., Rochester, N. Y., 14618.

NORTH CAROLINA CHAPTER OF ACR.
Secretary-Treasurer, Dr. Ira Bell, Hickory, N. C.

NORTH CAROLINA RADIOLOGICAL SOCIETY
Secretary, Dr. E. H. Schultz, North Carolina Memorial Hospital, Chapel Hill, N. C. Meets in the spring and fall each year.

NORTH DAKOTA RADIOLOGICAL SOCIETY
Secretary, Dr. A. Ohrt, 408 Medical Arts Bldg., Fargo, N. D. 58102. Meets at time of State Medical Association meeting. Other meetings arranged on call of the President.

NORTH FLORIDA RADIOLOGICAL SOCIETY
Secretary, Dr. Charles H. Newell, 800 Miami Road, Jacksonville 7, Fla. Meets quarterly in March, June, September and December.

NORTHEASTERN NEW YORK RADIOLOGICAL SOCIETY
Secretary, Dr. Herbert F. Reilly, Jr., 12 Sandalwood Rd., Scotia, New York 12302. Meets in Albany area on third Wednesday of October, November, March, April, and May.

NORTHERN CALIFORNIA RADIOLOGICAL SOCIETY
Secretary-Treasurer, Ivan D. Siddons, 3701 J. St., Suite 106, Sacramento, Calif. 95816. Meets fourth Monday of Sept., Nov., Jan., March and May at the Sutter Club in Sacramento.

NORTHWESTERN OHIO RADIOLOGICAL SOCIETY
Secretary, Dr. Vito J. Zupa, Mercy Hospital, Department of Radiology, Toledo, Ohio.

OHIO STATE RADIOLOGICAL SOCIETY
Secretary, Dr. Robert D. Berkebile, Elyria Memorial Hospital, Elyria, Ohio 44035.

OKLAHOMA STATE RADIOLOGICAL SOCIETY
Secretary, Dr. Donald F. Mauritson, 100 Utica Square Med. Center, Tulsa, Okla. 74114. Meets in January, May and October.

ORANGE COUNTY RADIOLOGICAL SOCIETY
Secretary, Dr. George W. Logan, 301 Newport Blvd., Newport Beach, Calif. Meets fourth Tuesday of every month at Orange County Medical Association Building.

OREGON RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Clinton B. Sayler, 214 Medical Dental Bldg., Portland, Oregon 97205. Meets on second Wednesday of month, October through April, at the University Club, Portland, Ore.

ORLEANS PARISH RADIOLOGICAL SOCIETY
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans, La. 70113. Meets second Tuesday of each month.

PACIFIC NORTHWEST RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Marvin Wallace, 555 108th Ave. N. E., Bellevue, Washington 98004.

PENNSYLVANIA RADIOLOGICAL SOCIETY
Secretary, Dr. Theodore A. Tristan, Harrisburg, Polyclinic Hosp., Harrisburg, Pa. 17105.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. C. Jules Rominger, Misericordia Hospital, 54th St. and Cedar Ave., Philadelphia, Pa. 19143. Meets first Thursday of each month at 5 P.M., from October to May in Thompson Hall, College of Physicians.

PITTSBURGH ROENTGEN SOCIETY
Secretary, Dr. Edward R. Seitz, 601 Jenkins Bldg., Pittsburgh, Pa. 15222. Meets second Wednesday of month, October through June, at Park Schenley Restaurant.

RADIATION RESEARCH SOCIETY
Secretary-Treasurer, Dr. Gail D. Adams, Dept. of Radiology, Univ. of Oklahoma Medical Center, Oklahoma City, Oklahoma 73104.

RADIOLOGICAL SOCIETY OF CONNECTICUT, INC.
Secretary-Treasurer. Dr. Henry J. Fox, 10 Washington Ave., Bridgeport, Conn. Meetings are held quarterly.

RADIOLOGICAL SOCIETY OF GREATER CINCINNATI
Secretary-Treasurer, Dr. Donald E. Gunderson, 3553 Bayard Dr., Cincinnati, Ohio 45208. Meets first Monday of each month at Cincinnati Academy of Medicine.

RADIOLOGICAL SOCIETY OF GREATER KANSAS CITY
Secretary, Dr. J. Stewart Whitmore, 1010 Rialto Bldg., Kansas City, Mo. Meets last Friday of each month.

RADIOLOGICAL SOCIETY OF KANSAS CITY
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

RADIOLOGICAL SOCIETY OF LOUISIANA
Secretary, Dr. Lester W. Eavenson, 2700 Napoleon Ave, New Orleans 15, La. Meets semiannually, during Louisiana State Medical Society meeting and 6 months later.

RADIOLOGICAL SOCIETY OF NEW JERSEY
Secretary, Dr. John W. Marquis, 12 Hawthorne Ave., East Orange, N. J. 07018. Meets in Atlantic City at time of State Medical Society meeting and in October or November in Newark, N. J.

RADIOLOGICAL SOCIETY OF RHODE ISLAND
Secretary-Treasurer, Dr. John M. Vesey, 1196 Elmwood Ave., Cranston, R. I.

Radiological Society of South Dakota
Secretary-Treasurer, Dr. Donald J. Peik, 303 S. Minnesota Ave., Sioux Falls, S. D.

Radiological Society of Southern California
Secretary-Treasurer, Dr. Robert G. Williams, The Santa Barbara Medical Clinic, P.O. Box 1200, Santa Barbara, Calif. 93102. Meets three times a year, usually October, February and May.

Radiological Society of the State of New York
Secretary-Treasurer, Dr. John W. Colgan, 273 Hollywood Ave., Rochester, N. Y. 14618.

Redwood Empire Radiological Society
Secretary, Dr. Lee F. Titus, 164 W. Napa St., Sonoma, Calif. Meets second Monday every other month.

Richmond County Radiological Society
Secretary, Dr. W. F. Hamilton, Jr., University Hospital, Augusta, Ga. Meets first Thursday of each month at various hospitals.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. Kenneth E. Robinson, Rochester General Hospital, 1425 Portland Ave., Rochester, N. Y. 14621. Quarterly meetings on the call of the President, at the Rochester Academy of Medicine.

Rocky Mountain Radiological Society
Secretary-Treasurer, Dr. Robert W. Lackey, 4200 E. Ninth Ave., Denver, Colo. 80220. Annual meeting: Brown Palace Hotel, Denver, Colo., Aug. 21–23, 1969.

San Antonio-Military Radiological Society
Secretary, Dr. Hugho F. Elmendorf, Jr., 730 Medical Arts Bldg., San Antonio 5, Tex. Meets third Wednesday of each month in Fort Sam Houston Officer's Club at 6:30 P.M.

San Diego Radiological Society
President-Secretary, Charles R. Henkelmann, 3909 Palm Drive, Bonita, Calif. 92002. Meets first Wednesday of each month at the Town & Country Motel.

San Francisco Radiological Society
Secretary-Treasurer, Dr. Walter W. Herbert, Saint Francis Memorial Hospital, 900 Hyde St., San Francisco, Calif. 94109. Meets quarterly at the San Francisco Medical Society, 250 Masonic Ave., San Francisco, Calif. 94118.

Santa Clara County Radiological Society
Secretary, Dr. D. Brendan O'Donnell, 696 E. Santa Clara St., San Jose, Calif. 95112. Meets monthly at the Santa Clara County Medical Association Bldg., 700 Empey Way, San Jose, Calif.

Section on Radiology, California Medical Association
Secretary, Dr. William H. Graham, 630 East Santa Clara St., San Jose, Calif.

Section on Radiology, Medical Society of the District of Columbia
Secretary-Treasurer, Dr. Louis Wener, Cafritz Memorial Hosp., 1310 Southern Ave., S.E., Washington, D. C. 20032. Meets at Medical Society Library, third Wednesday of January, March, May and October at 8:00 P.M.

Section on Radiology, Southern Medical Association
Secretary, Dr. Phillip W. Voltz, Jr., 120 Medical Professional Bldg., San Antonio, Texas 78212. Annual meeting: To be announced.

Section on Radiology, Texas Medical Association
Secretary, Dr. George F. Crawford, St. Elizabeth Hospital, Beaumont, Tex. Meets annually with the Texas Medical Association.

Shreveport Radiological Club
Secretary, Dr. W. R. Harwell, 608 Travis St., Shreveport, La. Meets monthly on third Wednesday at 7:30 P.M., September to May inclusive.

Society for Pediatric Radiology
Secretary, Dr. John L. Gwinn, Children's Hospital, 4614 Sunset Blvd., Los Angeles 27, Calif. Annual meeting: Washington-Hilton Hotel, Washington, D.C., September 29, 1969.

Society of Nuclear Medicine
Secretary, Mr. C. Craig Harris, Oak Ridge National Laboratories, Oak Ridge, Tenn. *Administrator*, Mr. Samuel N. Turiel, 430 N. Michigan Ave., Chicago 11, Ill. Annual meeting Jung Hotel, New Orleans La., June 22–28, 1969.

South Bay Radiological Society
Secretary, Dr. Emerson C. Curtis, University Dr., Menlo Park, Calif. 94025. Meets second Wednesday of each month.

South Carolina Radiological Society
Secretary, Dr. George W. Brunson, 1406 Gregg St., Columbia, S. C. Annual meeting (primarily business) in conjunction with the South Carolina Medical Association meeting in May. Annual fall scientific meeting at time and place designated by the president.

South Dakota Radiological Society
Secretary, Dr. Donald J. Peik, 1417 S. Minnesota Ave., Sioux Falls, S. Dak. Meets in spring with State Medical Society and in fall.

Southern California Radiation Therapy Society
Secretary-Treasurer, Dr. Aaron G. Fingerhut, 1000 W. Carson St., Torrance, Calif. 90502. Meets quarterly.

Southern Radiological Conference
Secretary-Treasurer, Dr. Marshall Eskridge, Mobile Infirmary, P.O. Box 4097, Mobile, Ala. 36604. Annual meeting: Grand Hotel, Pointe Clear, Ala. 36564, Jan. 31–Feb. 2, 1969.

Southwestern Radiological Society
Secretary, John M. McGuire, 904 Chelsea, El Paso, Tex. Meets last Monday of each month at 6:30 P.M. in the Paso del Norte Hotel.

Tennessee Radiological Society
Secretary-Treasurer, Dr. Marion E. Spurgeon, Memorial Hosp., Clarksville, Tenn. 37040. Meets annually at the time and place of the Tennessee State Medical Association meeting.

Texas Radiological Society
Secretary, Dr. Herman C. Sehested, 815 Medical Arts Bldg., Fort Worth 2, Tex. Annual meeting to be announced.

Tri-State Radiological Society
Secretary, Dr. John H. Marchand, Jr., Methodist Hospital, Henderson, Ky. Meets third Wednesday of Oct., Jan., March and May, 8:00 P.M., Elks Club in Evansville, Ind.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7:00 P.M. at University Hospital, Ann Arbor Mich.

Upper Peninsula Radiological Society
Secretary, Dr. A. Gonty, Menominee, Mich. Meets quarterly.

Utah State Radiological Society
Secretary-Treasurer, Dr. Leon M. Neal, St. Benedict's Hospital, 3000 Polk Ave., Ogden, Utah 84403. Meets fourth Wednesday in January, March, May, September and November at Holy Cross Hospital.

Vermont Radiological Society
Secretary, Dr. John R. Williams, 160 Allen St., Rutland, Vt.

Virginia Radiological Society
Secretary-Treasurer, Dr. K. Kenneth Wallace Jr., Norfolk, Va.

Washington State Radiological Society
Secretary-Treasurer, Dr. Paul S. Paulson, 1001 Broadway, Seattle, Washington 98122. Meets quarterly.

West Virginia Radiological Society
Secretary-Treasurer, Dr. George G. Green, Department of Radiology, W. Va. Univ. Medical Center, Morgantown, W. Va. 26506. Meets concurrently with Annual Meeting of West Virginia State Medical Society; other meetings arranged by program committee.

Westchester County Radiological Society
Secretary, Dr. Arnold Gerson, Medical Arts Bldg., Mt.

Vernon, N. Y. Meets on third Tuesday of January and October and on two other dates.

WISCONSIN RADIOLOGICAL SOCIETY
Secretary-Treasurer Dr. Robert E. Douglas, 117 N. Commerical St., Neenah, Wis. 54956. Meets twice a year, May and September.

WYOMING RADIOLOGICAL SOCIETY
Secretary, Dr. J. D. Grant, Memorial Hosp., Sheridan, Wyo. Meets in fall with State Medical Society and in spring on call of President.

CUBA, MEXICO, PUERTO RICO AND CENTRAL AMERICA

ASOCIACIÓN DE RADIÓLOGOS DE CENTRO AMERICA Y PANAMÁ. Comprising: Guatemala, El Salvador, Honduras, Nicaragua, Costa Rica and Panamá.
Secretary-General, Dr. Roberto Calderón, Calle Central Oeste No. 218, Managua, Nicaragua, Central America. Meets annually in a rotating manner in the six countries.

SOCIEDAD DE RADIOLOGÍA DE EL SALVADOR
Secretary, Dr. Julio Astacio, 5a Av. Nte. No. 434, San Salvador, Rep. El Salvador.

SOCIEDAD DE RADIOLOGÍA DE GUATEMALA
Secretary, Dr. Carlos E. Escobar, 9ª. Calle A 0-05, Zona 1, Guatemala.

SOCIEDAD DE RADIOLOGÍA Y FISIOTERAPÍA CUBANA
Secretary, Dr. Miguel A. García Plasencia, Hospital Curie, 29 y F, Vedado, Habana, Cuba. Meets monthly at Curie Hospital.

SOCIEDAD RADIOLOGICA COSTARRICENSE
Secretary, Dr. Carlos Cordero, Chavarri, Apartado VIII, San José, Costa Rica.

SOCIEDAD MEXICANA DE RADIOLOGÍA, A.C.
Coahuila No. 35, México 7, D. F.
Secretary-General, Dr. Ramón Ruenes.
Meets first Monday of each month.

ASOCIACIÓN PUERTORRIQUEÑA DE RADIOLOGÍA
Secretary, Dr. R. B. Díaz Bonnet, Suite 504, Professional Bldg., Santurce, Puerto Rico.

SOCIEDAD RADIOLÓGICA PANAMEÑA
Secretary, Dr. L. Arrieta Sánchez, Apartado No. 6323, Panamá, R. de P. Meets monthly in a department of radiology of a local hospital chosen at preceding meeting.

SOCIEDAD RADIOLÓGICA DE PUERTO RICO
Secretary, Dr. Felipe N. de Jesús, Apt. 9387, Santurce, Puerto Rico. Meets second Thursday of each month at 8:00 P.M. at the Puerto Rico Medical Association Bldg. in San Juan.

BRITISH COMMONWEALTH OF NATIONS

ASSOCIATION OF RADIOLOGISTS OF THE PROVINCE OF QUEBEC
Secretary, Dr. R. Robillard, Notre-Dame Hospital, 1560 Sherbrooke St., East, Montreal, Que., Canada. Meets four times a year.

BRITISH INSTITUTE OF RADIOLOGY
Honorary Secretary, Dr. G. H. du Boulay, 32 Welbeck St., London, W. 1, England. Meets monthly from October until May.

CANADIAN ASSOCIATION OF PHYSICISTS, DIVISION OF MEDICAL AND BIOLOGICAL PHYSICS.
Honorary Secretary-Treasurer, Paul M. Pfalzner, Department of Therapeutic Radiology, University of Western Ontario, London, Ontario, Canada.

EDMONTON AND DISTRICT RADIOLOGICAL SOCIETY
Secretary, J. D. R. Miller, M.B., University of Alberta Hospital, Edmonton, Alberta, Canada. Meets third Thursday of each month October to May, except December, at various Edmonton Hospitals.

FACULTY OF RADIOLOGISTS
Honorary Secretary, Dr. J. N. Pattinson, 47 Lincoln's Inn Fields, London, W.C.2, England.

FACULTY OF RADIOLOGISTS, ROYAL COLLEGE OF SURGEONS IN IRELAND
Registrar, Dr. H. O'Flanagan, F.R.C.P.I., D.P.H., 123 St. Stephens Green, Dublin 2, Ireland.

SECTION OF RADIOLOGY OF THE ROYAL SOCIETY OF MEDICINE (CONFINED TO MEDICAL MEMBERS)
Meets third Friday each month at 4:45 P.M. at the Royal Society of Medicine, 1 Wimpole St., London, W. 1, England.

CANADIAN ASSOCIATION OF RADIOLOGISTS
Honorary Secretary-Treasurer, Dr. Maurice Dufresne, *Associate Honorary Secretary-Treasurer*, Dr. F. Robert MacDonald, 1555 Summerhill Ave., Montreal 25, Que., Canada. Annual Meeting at the Hotel Vancouver, Vancouver, B.C., March 10–14, 1969.

MONTREAL RADIOLOGICAL STUDY CLUB
Secretary, Dr. Leonard Rosenthall, Montreal General Hospital, Montreal, Que., Canada. Meets first Tuesday evening, October to April.

SECTION OF RADIOLOGY, CANADIAN MEDICAL ASSOCIATION
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

SOCIÉTÉ CANADIENNE-FRANÇAISE DE RADIOLOGIE
Secretary General, Dr. Jacques Lespérance, 5415 Boul. L'Assomption, Montreal 26, P. Q., Canada. Meets every third Tuesday from October to April.

TORONTO RADIOLOGICAL SOCIETY
Secretary, Dr. George Wortzman, Toronto General Hosp., Toronto 12, Ont., Canada. Meets second Monday of each month, September through May.

COLLEGE OF RADIOLOGISTS OF AUSTRALASIA
Honorary Secretary, Dr. T. P. Loneragan, c/o British Medical Agency, 135 Macquarie St., Sydney, N.S.W., Australia.

SOUTH AMERICA

ASOCIACIÓN ARGENTINA DE RADIOLOGÍA
Secretary, Dr. Lidio G. Mosca, Avda. Gral. Paz 151, Córdoba, Argentina. Meetings held monthly.

ATENEO DE RADIOLOGIA
Secretary, Dr. Victor A. Añaños, Instituto de Radiologia, Santa Fe 3100, Rosario, Argentina. Meets monthly on second and fourth Fridays at 7:00 P.M. in the Hospital Nacional de Centenario, Santa Fe 1300, Rosario.

COLÉGIO BRASILEIRO DE RADIOLOGIA
Secretary-General, Dr. Miguel Mario Céntola, Caixa Postal 5984, São Paulo, Brazil.

SOCIEDAD ARGENTINA DE RADIOLOGIA
Secretary-General, Dr. Oswaldo E. Zerbo, Santa Fe 1171, Buenos Aires. Meetings are held monthly.

SOCIEDAD BOLIVIANA DE RADIOLOGÍA
Secretary, Dr. Javier Prada Méndez, Casilla 1182, La Paz, Bolivia. Meets monthly. General assembly once every two years.

SOCIEDADE BRASILEIRA DE RADIOLOGIA
Secretary, Dr. Armando Rocha Amoédo, Cxa Postal 1532, Rio de Janeiro, Brazil. General Assembly meets every two years in December.

SOCIEDADE BRASILEIRA DE RADIOTERAPIA
Secretary, Dr. Oscar Rocha von Pfuhl, Av. Brigadeiro Luiz Antonio, 644, São Paulo, Brazil. Meets monthly on second Wednesday at 9:00 P.M. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

SOCIEDAD CHILENA DE RADIOLOGÍA
Secretary, Dr. Manuel Concha, Casilla 13426, Santiago, Chile. Meets fourth Friday of each month.

SOCIEDAD COLOMBIANA DE RADIOLOGIA
Secretary-General, Dr. Armando Uribe, Hospital Militar Central, Apartado aéreo No. 5804, Bogotá, Colombia. Meets last Thursday of each month.

SOCIEDAD ECUATORIANA DE RADIOLOGÍA Y FISIOTERAPÍA
Secretary, Dr. Carlos Palau, Av. Bogotá 206, Guayaquil, Ecuador.

SOCIEDAD PARAGUAYA DE RADIOLOGÍA
Secretary, Dr. Miguel González Addone, 15 de Agosto 322, Asunción, Paraguay.

SOCIEDAD PERUANA DE RADIOLOGIA
Secretary-General, Dra. Ladis Delpino, Instituto de Radiología "Cayetano Heredia" Hospital Arzobispo

Loayza, Lima, Perú. Meets monthly except during January, February and March.

Sociedad de Radiologica del Atlantico
Secretary, Dr. Raul Fernandez, Calle 40 #41–110, Baranquilla, Colombia. Society meets monthly at the Instituto de Radiología.

Sociedad de Radiología, Cancerología y Física Médica del Uruguay
Secretary-General, Dr. José Claussius, Av. Agraciada 1464, piso 13, Montevideo, Uruguay.

Sociedade de Radiología de Pernambuco
Secretary, Dr. Manoel Medeiros, Instituto de Radiologia da Faculdade de Medicina da Universidade do Recife, Caixa Postal 505, Pernambuco, Brazil.

Sociedad de Roentgenología y Medicina Nuclear de la Provincia de Córdoba
Secretary-General, Dr. Lucas C. Di Rienzo, Ave. Grl. Paz. 151, Córdoba, Argentina.

Sociedad Venezolana de Radiología
Secretary-General, Dr. Modesto Rivero Gonzáles, Apartado No. 9362 Candelaria, Caracas, Venezuela. Meets monthly, third Friday at Colegio Médico del Distrito Federal, Caracas.

Continental Europe

Österreichische Röntgen-Gesellschaft
President, Dr. Konrad Weiss, Mariannengasse 10, Vienna 9, Austria. Meets second Tuesday of each month in Allgemeine Poliklinik.

Société Royale Belge de Radiologie
General Secretary, Prof. Simon Masy, Louvain, Belgium. Meets in February, March, May, June, September, October, November and December.

Société Européenne de Radiologie Pédiatrique
Permanent Secretary, Dr. Jaques Sauvegrain, Hôpital des Enfants-Malades, 149, rue de Sèvres, Paris 15e, France.
General Secretary, Dr. H. Ludin, Department of Roentgenology, Basler Kinderspital, Basel, Switzerland. Annual meeting: Warsaw, Poland, May 22–24, 1969.
Secretary, Dr. Kasawery Rowinski, Zaklad Radiologii Pediatrycznej Akademii Medycznej, Marzalkowska 24, Warszawa, Poland.

Société Française d'Electroradiologie Médicale, and its branches: Société du Sud-Ouest, du Littoral Méditerranéen, du Centre et du Lyonnais, du Nord, de l'Ouest, de l'Est, et d'Alger et d'Afrique du Nord. Central Society meets third Monday of each month, except during July, August and September, rue de Seine 12, Paris, France.
Secretary-General, Dr. Ch. Proux, 9 rue Daru Paris 8e, France.

Československá Společnost pro Roentgenologii a Radiologii
Secretary, Dr. Robert Poch, Praha 12, Srobárova 50, Czechoslovakia. Meets monthly except during July, August and September. Annual general meeting.

Deutsche Röntgengesellschaft
President, Professor Dr. med. Hanno Poppe, Radiologische Univ.-Klinik, Gossler Str. 10, 34 Göttingen, Germany.

Società Italiana di Radiologia Medica e di Medicina Nucleare
Secretary, Dr. Ettore Conte, Ospedale Mauriziano, Torino, Italy. Meets annually.

Nederlandse Vereniging voor Radiologie
Secretary, Dr. C. B. A. J. Puijlaert, Prof. Dondersstraat 73, Tilburg, Netherlands.

Scandinavian Radiological Society
Secretary-General, Dr. C. E. Unnérus, Professor, Hagalund-Tapiola, Havsvindsvägen 5 C., Finland. Annual meeting.

Sociedad Española de Radiología y Electrología Médicas y Medicina Nuclear
Secretary, Juan Gomez Lopez, Villanueva, 11, Madrid 1. Meets every second Friday of each month, Oct. to June, inclusive, in Madrid.

Schweizerische Gesellschaft für Radiologie und Nuklearmedizin (Société Suisse de Radiologie et de Médecine Nucléaire)
Secretary, Dr. Max Hopf, Effingerstrasse 47, Bern, Switzerland.

Asia

Indian Radiological Association
Secretary, Dr. R. F. Sethna, Navsari Building, Hornby Road, Bombay 1, India.

Indonesian Radiological Society
Secretary, Professor Sjahriar Rasad, Taman Tjut Mutiah I Diakarta, Indonesia

Iranian Radiological Society
Secretary, Dr. Issa Yaghmai, P.O. Box No. 14-1151, Teheran, Iran. The Society meets on the second Saturday of each month.

ABSTRACTS OF RADIOLOGICAL LITERATURE

INDEX TO ABSTRACTS

ROENTGEN DIAGNOSIS

HEAD

SCHOBER, R., and BENDER, R.: Orbital phlebography 230

DARLING, D. B., FEINGOLD, M., and BERKMAN, M.: The roentgenological aspects of Goldenhar's syndrome (oculoauriculovertebral dysplasia) 230

MAWDSLEY, C. *et al.*: Thermography in occlusive cerebrovascular diseases 231

GRABOW, J. D.: The role of neuroroentgenology in electrode placement technics in electroencephalography 231

NECK AND CHEST

NICOLESCO, N.: Radiological findings in pneumonia caused by Friedländer's bacilli; as noted in 62 cases 232

MATSANIOTIS, N. *et al.*: Idiopathic pulmonary hemosiderosis in children 232

SLADEN, A., LAVER, M. B., and PONTOPPIDAN, H.: Pulmonary complications and water retention in prolonged mechanical ventilation. 233

BROOKS, M. H. *et al.*: Acute pulmonary edema in falciparum malaria: clinicopathological correlation 233

SHEERS, G., and TEMPLETON, A. R.: Effects of asbestos in dockyard workers 234

LITTLE, J. M., and LOEWENTHALL, J.: Factors contributing to lowered mortality from pulmonary embolism 234

NORTHWAY, W. H., JR., and ROSAN, R. C.: Radiographic features of pulmonary oxygen toxicity in the newborn: bronchopulmonary dysplasia 234

VIALLET, P. *et al.*: Comparison of findings by angiography and scintigraphy in pulmonary pathology 235

CORNELL, S. H., VLAD, P., and EHRENHAFT, J. L.: Angiographic and catheterization findings in patients with difficulties after total correction of tetralogy of Fallot 235

DEVERALL, P. B.: Smooth-muscle tumors of the esophagus 236

MILLER, J. D., and HOWIE, P. W.: Traumatic rupture of the diaphragm after blunt injury.. 236

ABDOMEN

WEBB, D. I. *et al.*: Mechanism of vitamin B_{12} malabsorption in patients receiving colchicine 237

GROTH, C. G. *et al.*: Radioisotope scanning in experimental and clinical orthotopic liver transplantation 237

PAYNE, R. F.: Drip infusion cholangiography.. 238

TURNER, F. W., and COSTOPOULOS, L. B.: Percutaneous transhepatic cholangiography: a study of 115 cases 239

TRÉHEUX, A. *et al.*: The significance of intravenous cholangiography associated with duodenography in the study of the ampulla of Vater and chronic pancreatitis 239

GYNECOLOGY AND OBSTETRICS

GROS, CH., WALTER, J. P., and DELLENBACH, P.: Radiologic diagnosis of fetal death 240

KATTAN, K. R., and SPITZ, H. B.: Roentgen findings in obstetrical injuries to the brachial plexus 240

GENITOURINARY SYSTEM

NEMOY, N. J., and FORSBERG, L.: Polycystic renal disease presenting as medullary sponge kidney 240

BECKER, J. A., WEISS, R. M., and LATTIMER, J. K.: Renal tuberculosis: role of nephrotomography and angiography 241

BRIJS, A.: Extravasates with intravenous urography 241

MAXWELL, M. H., and LUPU, A. N.: Excretory urogram in renal arterial hypertension 242

WINTER, C.C. *et al.*: Radioisotope renography in assessment of renal function in newborn.. 242

FIGUEROA, J. E. *et al.*: Radioisotope renal function studies in human renal allografts: value in differential diagnosis of oliguria in presence of obstructive disease with and without urinary extravasation 243

BROOKS, V., and BATESON, E. M.: Cystourethrography in the University Hospital of the West Indies 243

BRANDTLOW, K.: Urethrocystography 243

SKELETAL SYSTEM

CARROLL, T. B., and GRUBER, J. H.: Seat belt fractures: a report of two cases 244

Friendenberg, Z. B., and Kohanim, M.: The effect of direct current on bone..... 244
Allen, E. H., Millard, F. J. C., and Nassim, J. R.: Hypo-hyperparathyroidism..... 244
Boström, H. *et al.*: Metabolic and orthopedic treatment of a case of adult nonfamiliar hypophosphatemia with severe osteomalacia 245
Galasko, C. S. B. *et al.*: Use of the gamma camera for early detection of osseous metastases from mammary cancer..... 245

Blood and Lymph System

Dotter, C. T., Rösch, J., and Judkins, M. P.: Transluminal dilatation of atherosclerotic stenosis..... 246
Lebouchard, R. *et al.*: The significance of occlusive phlebography in the evaluation of therapeutic portocaval anastomoses..... 246
Son, Y. H., Wetzel, R. A., and Wilson, W. J.: ^{99m}Tc pertechnetate scintiphotography as diagnostic and follow-up aids in major vascular obstruction due to malignant neoplasm..... 247
Broussin, J., and Martin, P. L.: Addition to counter-current arteriography..... 247

General

Gondos, B.: Roentgen observations in diabetic osteopathy..... 248
Razzak, M. A., Hassaballa, A. M., and Abou-Khatwa, H.: Evaluation of the peripheral circulation in diabetics by means of a modified radioisotopic technic..... 248

RADIATION THERAPY

Goldberg, B. B., Sklaroff, D. M., and Isard, H. J. Echoencephalography in the management of patients receiving radiation therapy..... 249

CHEMOTHERAPY

Wolff, J. A. *et al.*: Single versus multiple dose dactinomycin therapy of Wilms' tumor.... 249
Kennedy, B. J.: Progestogens in the treatment of carcinoma of the endometrium..... 250

ROENTGEN DIAGNOSIS

HEAD

SCHOBER, R., and BENDER, R. Orbita-phlebographie. (Orbital phlebography.) *Fortschr. a. d. Geb. d. Röntgenstrahlen u. d. Nuklearmedizin*, Sept., 1968, *109*, 345–360. (Address: Professor Dr. med. R. Schober, Chefarzt des Zentral-Röntgeninstitutes und der Strahlenabteilung Städt. Krankenhaus, 52 Siegburg, Germany.)

Unilateral exophthalmus usually is the result of a space occupying mass within the orbit. Conventional roentgenography does not yield a valuable clue and only occasionally is a localized bone erosion or a widened fissure detected. When the increased pressure persists for long periods, the entire orbit may become enlarged. Rarely encountered small calcifications indicate the site of the lesion but not its nature. Air insufflation into Tenon's capsule or the retrobulbar tissues combined with tomograms are helpful for localization. This procedure, however, is painful and may lead to intraorbital adhesions and even blindness. Carotid angiograms usually demonstrate the ophthalmic artery but are of limited value at best.

Venography, on the other hand, is more suitable and informative. The angular vein and the superior and inferior ophthalmic veins present with a characteristic pattern so that deviations can easily be recognized. There are 2 techniques of performing orbital phlebography: (1) percutaneous needle puncture of the angular vein with simultaneous compression of the facial vein; and (2) introduction of an ultrathin catheter through a tiny incision of the skin. The latter technique is preferable as the head can be freely manipulated for proper positioning and paravasates do not occur. The catheter can be connected with a mechanical device so that the operator remains protected. A minute residual scar is negligible.

Ten ml. of a water soluble 60 per cent contrast material is slowly injected while biplane exposures are made during a period of 8 seconds. The most informative views are obtained with the frontal and lateral projections. Compression of the frontal and nasofrontal veins is immaterial and even disadvantageous as it prevents a shunt when drainage via the cavernous sinus is blocked. Without compression, also a normal contralateral orbital venogram becomes available for comparison in the frontal view. The injection causes a transient sensation of localized heat but no complications.

For diagnostic conclusions, the frontal view is more revealing than the lateral. Dividing the all important superior ophthalmic vein into the perbulbar, the middle and the postbulbar segments aids in the localization of a mass. Usually, only one segment of the artery is predominantly involved. Characteristic abnormal findings are stenosis or complete thrombotic obstruction with prestenotic dilatation and development of collateral circulation. As a result, the blood flow is shunted away from the cavernous sinus to the facial veins and the contralateral orbit. Such reversal together with vessel displacement is more pronounced in neoplasms than in inflammatory processes. The latter, on the other hand, tend to cause an increase and dilatation of the veins. In tumors, this only occurs after collaterals have developed following thombotic occlusion or stenosis of the vein. Tumor vessels may also simulate collateral circulation.

Space occupying masses can be well enough localized to plan surgical procedures, but the nature of the lesions still offers differential diagnostic difficulties. A less characteristic displacement pattern, increased vascularization and normal drainage to the cavernous sinus suggest an inflammatory process rather than a neoplasm.

The phlebographic findings are illustrated in 6 tumors and 2 inflammatory conditions.—*Ernest Kraft, M.D.*

DARLING, D. B., FEINGOLD, MURRAY, and BERKMAN, MILTON. The roentgenological aspects of Goldenhar's syndrome (oculoauriculovertebral dysplasia). *Radiology*, Aug., 1968, *91*, 254–260. (From: New England Medical Center Hospitals, 171 Harrison Avenue, Boston, Mass. 02111.)

Goldenhar's syndrome or oculoauriculovertebral dysplasia was first described by van Arlt in 1845. Thus far, including the 2 presently discussed patients, the total number of cases reported is 48.

Clinically the principal features are: (a) epibulbar dermoids (the most constant finding) or lipodermoids; (b) auricular appendices and pretragal, blind-ended fistulas; and (c) vertebral anomalies.

The epibulbar dermoid is located in the outer lower quadrant of the eye at the limbus or corneal margin. The lipodermoid occurs in the upper outer quadrant. Other ocular findings are unilateral upper lid coloboma, anophthalmia, microphthalmia, and microcornea.

Another constant finding is the preauricular appendices which occur along a line from the tragus to the angle of the mouth. These are usually bilateral and frequently multiple. Microtia and deficiency of the external auditory meatus occur.

Oral manifestations include micrognathia and/or unilateral hypoplasia of the mandible. Bifid tongue, bifid uvula, double frenulum, high palate and cleft lip have been described.

Vertebral anomalies are common and include occipitalization of the atlas, fused vertebrae, hemi-

vertebrae, spina bifida, supernumerary vertebrae, scoliosis, and sacral fovea.

The major areas of interest roentgenographically are the mandible, maxilla, temporal bone and vertebral column. Mandibular changes vary from minor asymmetry to marked hypoplasia of the ramus and condyle. The facial bones also show unilateral hypoplasia. Vertebral anomalies were found in 2 of 6 patients with elongation of the odontoid and cephalad articulation of the tip with the arch of C-1.

Both Treacher-Collins syndrome and hemifacial microsomia can be distinguished from oculoauriculovertebral dysplasia by their lack of epibulbar dermoids and lack of vertebral anomalies.—*John P. Eberts, M.D.*

Mawdsley, C., Samuel, E., Sumerling, M. D., and Young, G. B. Thermography in occlusive cerebrovascular diseases. *Brit. M. J.*, Aug. 31, 1968, *3*, 521–524. (Address: Dr. C. Mawdsley, Senior Lecturer in Neurology, Edinburgh University, Edinburgh, Scotland.)

The possibility of effective treatment provides a stimulus for a more precise screening diagnostic technique for extracranial lesions of the carotid and vertebral systems.

Facial thermography has a place in the investigation of cerebral vascular disease. It may be safely carried out, even in ill or bedfast patients. It causes the patients no discomfort and gives rapid results which are easily interpreted. As a useful screening test, it therefore has some advantages over other methods such as angiography, echoencephalography, ophthalmodynamometry.

Human skin is an almost perfect absorber and emitter of infrared energy between the wave lengths of 3 and 15 microns. If the temperature of the environment is controlled, the temperature of the skin fluctuates, mainly because of skin blood flow.

The skin of the face is largely supplied by the external carotid artery, but the medial part of the forehead above the inner aspect of the orbit on each side is supplied by the frontal and supraorbital branches of the ophthalmic artery. This arises from the internal carotid artery just after it emerges from the cavernous sinus. A lesion of the internal carotid artery proximal to the origin of the ophthalmic artery which is sufficient to cause reduced blood flow might be expected to lead the cooling over the central part of the forehead on the corresponding side.

Thermal maps of patient's faces were obtained with the Aga-Thermovision 652. This apparatus detects infrared radiation by means of an indium-antimonide junction cooled by liquid nitrogen. Detailed description of its construction is presented. The thermogram appears as a continuous range of grey tones on a polaroid film.

A total of 125 patients were studied; 72 patients were also studied angiographically, and 53 were not. The thermographic findings in these patients are summarized in detail.

The thermographic changes did not tally with the angiographic findings in 21 patients; that is, nearly 30 per cent of the total. However, in the presence of severe stenosis or complete occlusion of one carotid artery proximal to the origin of the ophthalmic artery, there was an 82 per cent correlation between the thermographic diagnosis and the arterial lesion demonstrated radiographically. This figure is similar to Woods' (1965), 88 per cent, and Aarts' (1960), 95 per cent.

Both of these authors, as the authors of this series, found that significant cooling of the forehead occurred when the lumen of the carotid artery was reduced by about 50 per cent. These changes are at variance with the experimental work of Hamilton in dogs, and Brice in humans. These investigators found that the blood flow was reduced by arterial stenosis only if the arterial lumen was reduced by a factor of 84 to 93 per cent. The discrepancy in these findings is discussed. Turbulent flow produced by irregular contours of atheroma is suggested as a possible explanation.

There are limitations of thermography. Facial thermography is of little use in the presence of vertebral basilar arterial disease. Misleading "false positive" findings occurred fairly commonly. Minor degrees of carotid stenosis are not revealed. The causes of inaccuracy are not always clear. Variations in the size of the frontal sinuses produce some variations in the thermal pattern over the forehead. Pyrexia, local inflammatory lesions, bilateral disease of the carotid arteries, and stenosis of the ophthalmic artery itself are all potential sources of error.

Despite these drawbacks, it is concluded that facial thermography has a place in the investigation of the cerebral vascular disease.—*William T. McLaughlin, M.D.*

Grabow, Jack D. The role of neuroroentgenology in electrode placement technics in electroencephalography. *Radiology*, Sept., 1968, *91*, 501–507. (From: Department of Neurology, University of Wisconsin Medical Center, Madison, Wis. 53706.)

The usefulness of neuroroentgenology to the electroencephalographer in determining the exact position of scalp, nasopharyngeal, sphenoidal, and depth electrodes is discussed. Also, this report is intended to acquaint the neuroroentgenologist with some of the electrode recording techniques employed in electroencephalography and to encourage the

further use of roentgenology by electroencephalographers.

In scalp recording, after localizing the spike discharge by phase reversal techniques, roentgenograms should be obtained. This allows more accurate correlation between the clinical seizure and abnormal focus location and provides more precise follow-up information. Furthermore, the neurosurgeon can better visualize the extent of the craniotomy if roentgenograms accompany the electroencephalographic reports.

Three cases are reported, illustrating this technique.

In addition, nasopharyngeal and sphenoidal electrodes can be located relative to the anatomy by this technique. In the case of the multicontact depth probe, the roentgenograms give the precise cerebral location of the epileptogenic activity and allow better correlation between brain pathology and electrical activity at the different probe contacts. —*L. H. Deiterman, Jr., M.D.*

NECK AND CHEST

NICOLESCO, N. Constations radiologiques au cours des pneumonies à bacilles de Friedländer: observations portant sur 62 cas. (Radiologic findings in pneumonia caused by Friedländer's bacilli; as noted in 62 cases.) *J. de radiol., d'électrol. et de méd nucléaire*, June-July, 1968, *49*, 451–464. (From: Clinique I et II des maladies infectieuses de Bucarest, Romania.)

The author states that roentgenography is a unique and dependable method pointing to an early diagnosis of Friedländer's pneumonia. The maximum incidence is between the ages of 40 to 60 years (35 cases out of 62).

The roentgen manifestations even though varied have the following consistent characteristics: The pulmonary lesions can be observed very early within 24 to 48 hours after the start of symptoms. These lesions suppurate rapidly and hence large cavities are formed within a few days. About 55 per cent present completely opacified lobes characterized by intense pneumonic condensation involving numerous segments of the lobe or even the entire lobe. They are mostly unilateral and very rarely bilateral. These so-called black pneumonic blocks can further be subdivided according to their appearance, the most prevalent being the pseudocystic type, wherein the condensation has more or less an ovoid or round configuration resembling a cyst. Less frequently, pseudotumoral and triangular or bronchopneumonic configuration of consolidation are noted. About 15 per cent of cases present a bronchopneumonic roentgen appearance and about 29 per cent present atypical roentgen characteristics. Rapid suppuration, noted in all the intensely condensed pneumonic forms may cause displacement of the adjacent mediastinal structures and trachea because of increased pressure within the lobe. The pseudotumoral forms usually show a polycyclic contour with well delineated boundaries along the interlobar pleural spaces. The triangular pneumonic form also presents rather sharp zonal boundaries of condensation, even though the condensation may not be homogeneous.

The bronchopneumonic pseudolobar forms give the impression of multifocal pneumonia. Tomographic studies in such cases will always demonstrate clearly the nodular structure of these foci as well as very small and early cavity formation. Later larger cavity formations will be clearly demonstrated by conventional roentgenography. Early diagnosis and antibiotic administration may prevent the further extension of these inflammatory foci. Disseminated bronchopneumonic forms usually are noted in elderly patients with a background of emphysema and hypoventilation, as well as in patients who have had acute bronchitis of the viral type.

Atypical forms are noted in elderly patients as well as in children and do not present any characteristic roentgen appearance. They resemble ordinary bronchopneumonia. The diagnosis in such cases is bacteriological.

Complications noted are spontaneous pneumothorax, pleural effusion, mediastinal and hilar lymphadenopathy. Residual cavity formations at times requiring surgical excision have been noted. Re-activation of pre-existing arrested tuberculosis can also be counted as a complication. Retraction deformity of hemithorax as a result of healed pneumonia due to Friedländer's bacilli has also been reported.

The prognosis is very serious in case of massive suppuration with gigantic cavity formations.

The differential diagnosis includes various cysts, sarcoma and encysted pyopneumothorax. The triangular condensation forms should be differentiated from regular pneumonic zonal or lobar condensations. The streptococcic pneumonia could also cause suppuration and cavitation; however, the fluid content of these cavities is not under pressure and a fluid level can be noted. Other types of pneumonia and fibrocaseous tuberculosis should be differentiated. Neoplastic metastases at times may simulate such pneumonic roentgen appearance.—*Jirair N. Sarian, M.D.*

MATSANIOTIS, N., KARPOUZAS, J., APOSTOLOPOULOU, E., and MESSARITAKIS, J. Idiopathic pulmonary hemosiderosis in children. *Arch. Dis. Childhood*, June, 1968, *43*, 307–309. (Address: Pediatric Clinic of Athens Uni-

versity, St. Sophie's Hospital, Athens, Greece.)

The subject of this article is a review of 26 cases of idiopathic pulmonary hemosiderosis—a disease predominantly of childhood. All patients had hypochromic microcytic anemia of variable severity and siderophages in the sputum or gastric washings. Roentgenologically diffuse homogeneous shadows were seen in the lungs of all patients during the acute phase. These infiltrates changed rapidly in size, density and distribution and usually cleared within 1–2 weeks.

The etiology of idiopathic pulmonary hemosiderosis is unknown. Various hypotheses are advanced: congenital weakness or fragility of lung capillaries; milk allergy; and immuno-allergy. The lung biopsy findings have shown hemorrhage with striking but nonspecific hemosiderosis and fibrosis.

The incidence of this condition is higher in Greece than elsewhere and of the 26 children presented here 13 originated from a small area of central Greece inhabited by an isolated community in which intermarriage is common. This supports the probability that hereditary factors may be involved in the development of idiopathic pulmonary hemosiderosis.

The prognosis is grave. Steroid therapy during the acute phase of the disease appears to speed up recovery and improve immediate prognosis. However, long-term steroid therapy does not seem to prevent crises or to prolong survival.

Of the 26 cases in this series, 20 have been followed up: 4 of these have died, 12 are on maintenance steroid therapy and 1 is free of symptoms.—*Lionel W. Young, M.D.*

Sladen, Arnold, Laver, Myron B., and Pontoppidan, Henning. Pulmonary complications and water retention in prolonged mechanical ventilation. *New England J. Med.*, Aug. 29, 1968, *279*, 448–453. (From: Respiratory Unit of the Anaesthesia Department and Anaesthesia Laboratories of Harvard Medical School at the Massachusetts General Hospital, Boston, Mass.)

In the management of respiratory failure it has been shown that acute deterioration of respiratory function frequently is accompanied by roentgenographic changes consistent with the diagnosis of pulmonary edema. There is often no peripheral edema, but there may be a weight gain or a failure to lose weight during a period of negative nitrogen balance. These changes occur with a fall in pulmonary compliance, a rise in the ratio of dead space to tidal volume and a widening of the alveolar-arterial oxygen tension difference.

The authors present a retrospective study of 100 patients treated with prolonged mechanical ventilation. Water retention without other evidence of cardiac failure developed in 19, and roentgenograms of the chest taken before diuretic therapy were interpreted varyingly as showing bilateral hazy, diffuse, or fluffy infiltrates or pulmonary edema. In 4 patients the changes were interpreted as pulmonary congestion. Following diuretic therapy, the roentgenogram showed either complete clearing or improvement. In 4 patients water retention was not associated with roentgenologic changes.

The authors conclude that the appearance of pulmonary edema may be related to a relative water overload, a rise in antidiuretic hormone production or subclinical cardiac failure. The sudden appearance of diffuse pulmonary edema in a ventilated patient should suggest the possibility of an increase in pulmonary extravascular water, but an associated increase in the alveolar-arterial oxygen tension difference, a rise in the ratio of wasted ventilation, and a fall in the estimated compliance and vital capacity are indicative of water retention with potentially lethal pulmonary complications.

The roentgenographic findings are easily reversible in the early phase but failure to recognize this syndrome may lead to a continuous downhill course consisting of progressive difficulty in oxygenation and ventilation.—*James R. Knapp, M.D.*

Brooks, Marion H., Kiel, Frank W., Sheehy, Thomas W., and Barry, Kevin G. Acute pulmonary edema in falciparum malaria: clinicopathological correlation. *New England J. Med.*, Oct. 3, 1968, *279*, 732–737. (From: The Department of Metabolism, Walter Reed Army Institute of Research, Department of Medicine, Walter Reed General Hospital and the Armed Forces Institute of Pathology, Washington, D. C.)

The clinical and autopsy findings in 5 patients with pulmonary edema due to acute falciparum malaria were correlated.

The clinical illness was characterized by a progressive deterioration, severe cerebral dysfunction, overt intravascular hemolysis and marked parasitemia. In all cases, rapidly lethal pulmonary edema, unresponsive to vigorous therapy, occurred in the absence of detectable cardiac decompensation or fluid retention.

The study does not completely elucidate the pathogenesis of pulmonary edema in malaria but the following hypothesis is offered: the acute phase of falciparum malaria is characterized by generalized vasodilatation with clinical manifestations of a decreased effective circulating blood volume. The attendant decrease in organ perfusion is further aggravated by local changes in the microcirculation. Aggregation of erythrocytes, diminished flow, increased capillary permeability and interstitial edema

occur sequentially as the infection progresses.—*Saul Heiser, M.D.*

SHEERS, GEOFFREY, and TEMPLETON, ANN R. Effects of asbestos in dockyard workers. *Brit. M. J.*, Sept. 7, 1968, *3*, 574–579. (Address: Dr. Geoffrey Sheers, Consultant Chest Physician, Plymouth General Hospital, Plymouth, England.)

The incidence of pleural and pulmonary abnormalities attributed to asbestos among 15,000 workers in a British Naval yard was studied by means of a 1 in 10 sample; 94 per cent of the men in the sample were examined. Of these, 3 per cent had experienced continuous occupational exposure to asbestos and half the remainder (representing approximately 6,800 men) had been exposed intermittently. The prevalence of chest abnormalities ranged from 28 per cent in continuously exposed workers to 1.9 per cent in those with least exposure.

The roentgenographic abnormalities attributed to asbestos are as follows: the commonest finding is a limited plaque (not exceeding the equivalent of 4 rib interspaces) of pleural thickening frequently with calcification seen best on the lateral chest wall; it is characteristically bilateral and does not involve the costophrenic angles. More extensive pleural thickening may also be seen with peripheral opacities overlapping the lung fields to varying degrees. Pulmonary fibrosis characterized by parenchymal nodular and linear opacities are less frequent and usually associated with pleural changes.

Most cases of pulmonary fibrosis occurred in laggers and sprayers who had been continuously exposed between 15 and 20 years. Pulmonary fibrosis was also seen in the variety of intermittently exposed trades and had been preceded by extensive pleural thickening in some cases.

Ten cases of pleural mesothelioma have occurred in the last 3 years and a large number of men appeared to be potentially at risk.—*Saul Heiser, M.D.*

LITTLE, J. M., and LOEWENTHALL, JOHN. Factors contributing to lowered mortality from pulmonary embolism. *Surg., Gynec. & Obst.*, Oct., 1968, *127*, 777–782. (From: The Department of Surgery, The University of Sydney and the Royal Prince Alfred Hospital, Sydney, Australia.)

Survey of the incidence and mortality of pulmonary embolism for the years 1964 and 1965 was done at the Royal Prince Alfred Hospital, Sydney, Australia. The groups were comparable as to age distribution and site of origin of the emboli. There was a distinct drop in the mortality statistics in 1965 which coincided with the institution of caval interruption. Additional factors in the decreased mortality were the earlier diagnosis and more aggressive treatment including the use of anticoagulants.

Of interest was the erroneous assumption that the patients with carcinoma who died of pulmonary emboli in 1964 were suffering from advanced cancer. Actually, only 4 of the 9 patients who died with pulmonary emboli in 1964 were in the terminal stages of disease. Among the patients offered caval interruption in 1965 were 3 suffering from a known malignant lesion. The general trend toward vigorous treatment of venous thrombosis in carcinoma patients is encouraged by the authors.—*Saul Heiser, M.D.*

NORTHWAY, WILLIAM H., JR., and ROSAN, ROBERT C. Radiographic features of pulmonary oxygen toxicity in the newborn: bronchopulmonary dysplasia. *Radiology*, July, 1968, *91*, 49–58. (Address: Dr. W. H. Northway, Jr., Stanford Medical Center, Palo Alto, Calif. 94304.)

Bronchopulmonary dysplasia is a new syndrome of pulmonary disease which is seen following prolonged oxygen and respiratory therapy of the respiratory distress syndrome of the newborn. It is believed to represent toxic manifestations of 80–100 per cent oxygen on the developing lung superimposed upon the healing phase of respiratory distress syndrome. This syndrome has been divided into 4 stages, based on clinical, roentgenologic, and pathologic findings. These 4 stages are as follows:

STAGE I. Clinically and roentgenographically resembles ordinary respiratory distress syndrome except for excessive mucosal necrosis (1 to 3 days of age).

STAGE II. Characterized by marked radiopacity of the lungs, inability to be weaned from high O_2, and cycles of alveolar injury and repair (4 to 10 days of age).

STAGE III. Roentgenographic cystic appearance of the lungs with respiratory mucosal lesions, focal emphysema and persistence of hyaline membranes, and gradual weaning from high O_2, (10 to 20 days of age).

STAGE IV. Symptomatic chronic lung disease predominant, with strands of pulmonary parenchymal density, increased thoracic volume, and cardiomegaly which may gradually clear or progress to cor pulmonale and death (beyond 1 month of age).

The authors present in detail the characteristic roentgenographic evolution of the pulmonary changes of this syndrome, based on the findings observed in 32 patients who required 24 hours or more continuous intermittent positive pressure respiration with high O_2 as a life-saving measure at the Stanford Premature Infant Research Center from September 1962 to November 1965. The

appearance of chronic lung disease—the late stage of bronchopulmonary dysplasia—was noted in only those infants who received more than 6 days of continuous high O_2 therapy and lived longer than 4 weeks.

The roentgenographic features in all infants of this series were indistinguishable from those of the "classical" respiratory distress syndrome of the newborn with bilateral fine granular densities in the lung and an air bronchogram being seen. The initial roentgenographic severity of the respiratory distress syndrome, as judged by the relative amount of pulmonary parenchymal density, did not appear increased in most cases in which the late stages of bronchopulmonary dysplasia developed. In the infants who survived beyond 3 days of age and who required continued high O_2 and respiratory therapy, increasingly dense coarse granular infiltrates developed in the lungs and these often obscured the cardiac margins. The major bronchi frequently appeared to be the only air containing structures in the chest. Between the 10th and 20th days of life (Stage III), when weaning from the respirator and high O_2 therapy was generally accomplished, small cyst-like foci appeared in the generally opaque lungs, and the cardiac borders again became identified. This picture changed after 1 month of age (Stage IV) to a lace-like pattern of alternating irregular cyst-like foci and strands of density with an apparent increase in the over-all thoracic volume.

All infants who survived beyond 4 weeks of age without development of clinical or roentgenographic chronic lung disease had received less than 6 days of high O_2 therapy and all showed clearing of the initial bilateral granular densities by the 4th week of life.

Apparent roentgenographic increase in cardiac size was not unusual during the course of early bronchopulmonary dysplasia. Only those infants with chronic lung disease both roentgenographically and clinically showed persistent cardiomegaly beyond 4 weeks of life, and all of these children eventually died with right sided congestive heart failure between the ages of 1 and 11 months.

The authors discuss the differential diagnosis and state that it is the evolution of the roentgenographic findings in bronchopulmonary dysplasia which distinguishes it from the pulmonary changes seen in the Mikity-Wilson syndrome or pulmonary dysmaturity, pulmonary lymphangiectasia, Hamman-Rich disease in infancy, or cystic fibrosis in infancy. None of these other diseases, however, characteristically shows the initial classical pattern of respiratory distress syndrome or the sequence of changes which bronchopulmonary dysplasia presents.

The authors also discuss in detail the clinical findings and the pathology of this syndrome.

Several case reports are presented along with reproductions of roentgenograms illustrating the findings seen in this syndrome.

It is felt that the roentgenographic evolution of pulmonary changes is characteristic and unique. Recognition and knowledge of this condition are important in the current management of respiratory distress syndrome of the newborn.—*Donald N. Dysart, M.D.*

VIALLET, P., MEYNIEL, G., MOLINA, C., PLAGNE, R., BRUN, J., and VIALLET, J. F. Confrontation des données de l'angiographie et de la scintigraphie en pathologie pulmonaire. (Clermont-Ferrand, France.) (Comparison of findings by angiography and scintigraphy in pulmonary pathology.) *J. de radiol., d'électrol. et de méd. nucléaire*, Aug.-Sept., 1968, *49*, 558–561.

After comparing the findings by angiography and scintigraphy in 30 patients (8 with malignant lesions, 22 with pulmonary dystrophies or sequelae from tuberculosis), the authors conclude that both methods are useful in determining pulmonary function, but that angiography is superior in giving evidence of the venous vasculature, shows affections of the heart and major vessels, and is more precise in delimiting malignant from unaffected tissue.

Scintigraphy on the other hand is completely innocuous and can be repeated as often as desired, so that evolution of a treated neoplasm can be followed; also, when plain roentgenograms show that reventilation has appeared, scintigraphy discloses whether revascularization has occurred simultaneously. Thus the 2 methods are complementary.—*Frank A. Riebel, M.D.*

CORNELL, STEVEN H., VLAD, PETER, and EHRENHAFT, JOHANN L. Angiographic and catheterization findings in patients with difficulties after total correction of tetralogy of Fallot. *Radiology*, Aug., 1968, *91*, 321–328. (Address: Dr. S. H. Cornell, Department of Radiology, University Hospitals, Iowa City, Iowa 52240.)

Tetralogy of Fallot is an anatomically complex intracardiac defect resulting in right-to-left or bidirectional shunts at the ventricular level and decreased pulmonary blood flow. The peripheral arterial unsaturation varies both with the size of the interventricular defect and its anatomic relation to the enlarged aortic root, and with the severity of the right ventricular outflow obstruction. Total repair of this anomaly achieves physiologic correction by separation of the intracardiac streams and by relief of the pulmonic stenosis. Total repair may or may not result in perfect anatomic or entirely normal intracardiac pressure relationships.

The authors report a series of 124 patients operated on, of whom there were 102 long-term survivors. Twelve of these were restudied by cardiac catheterization and angiocardiography from 2 months to 10 years after total correction of defects. Restudy of these patients was prompted by clinical, roentgenographic and electrocardiographic signs of persistent abnormality. The most common indication for re-examination was the presence of a loud systolic murmur over the pulmonary area suggesting a significant residual pulmonary stenosis. Other indications were a loud diastolic murmur or parasternal systolic murmur, cardiac enlargement and failure, roentgenographic findings suggestive of right ventricular outflow tract aneurysm, and electrocardiographic evidence of increasing right ventricular hypertrophy. The essential pre- and postoperative data are presented in tabular form and case reports of 7 of these patients are presented in detail.

The most common angiocardiographic finding in the group of 12 cases was residual infundibular stenosis which was seen in 10 patients. Other conditions encountered were: residual infundibular or valvular stenosis, increasing hypertrophy or enlargement of right ventricle, aneurysm of the right ventricular infundibulum, residual interventricular septal defect, previously undiagnosed atrial septal defect, subaortic stenosis, aortic insufficiency, stenosis of main pulmonary artery, and pulmonary insufficiency.

In this group of patients 3 were found to have hemodynamic and angiocardiographic evidence of significant residual abnormality. Each has had a repeat operation with good results. The remaining 9 patients are being followed at regular intervals and all are to have re-operations if their cardiac status deteriorates.

The authors emphasize that repeat catheterization and angiocardiography have identified the cause of persistently abnormal signs and symptoms in these patients and have made it possible to differentiate between those who require repeat surgery and those who could safely be followed.—*Edward B. Best, M.D.*

DEVERALL, P. B. Smooth-muscle tumors of the esophagus. *Brit. J. Surg.*, June, 1968, *55*, 457–461. (From: The Department of Thoracic Surgery, General Infirmary, Leeds, England.)

Smooth muscle tumors occur at all levels of the gastrointestinal tract, but their occurrence in the esophagus is considered to be rare. Only 200 cases have been described in the world literature.

Because of their essentially benign nature, recognition of these lesions is important, and the author reports 12 cases.

Postmortem examination of over 7,000 cases at the Mayo Clinic by Harrington and Moerisch (1944) revealed 44 cases of benign esophageal tumor. In the author's department, over the same 23 year period, 876 cases of esophageal carcinoma were seen, and the 12 cases of leiomyoma represent an incidence of about 1.5 per cent. The distribution of 53 per cent in the lower third, 35 per cent in the middle third, and 12 per cent in the upper third of the esophagus, compares favorably with other series.

The microscopic appearance of these tumors is that of a multilobular lesion resembling uterine fibromyomas.

The symptoms are variable but often are related to associated conditions such as gastric ulcer, hiatus hernia, etc.

Schatzki and Hawes (1950) and Harper and Tiscenco (1945) have reviewed the roentgenologic findings in detail. Barium swallow and meal are the most useful methods of examination. A smooth rounded filling defect with clearly demarcated edges is classical. The appearance may be bizarre and in some cases a lesion is not suspected, although associated with findings such as reflux and gastric herniation. In the author's series, abnormalities were present on a plain chest roentgenogram in 2 of the cases. Esophageal middle third tumors may become evident, although quite small, as prominences of the right mediastinal border just above the hilar region. In 1 case, mediastinal widening was caused by a huge tumor with esophageal dilatation.

Esophagoscopy is essential, and the findings are often diagnostic, particularly with middle third lesions.

In involvement of the lower third, these tumors are more often associated with other lesions and are more difficult to diagnose.

In the author's experience, the most satisfactory surgical procedure was enucleation of the tumor.—*James R. Knapp, M.D.*

MILLER, J. D., and HOWIE, P. W. Traumatic rupture of the diaphragm after blunt injury. *Brit. J. Surg.*, June, 1968, *55*, 423–428. (From: The Western Infirmary, Glasgow, Scotland.)

Blunt injury to the lower chest or abdomen may cause rupture of the diaphragm followed by herniation of abdominal contents into the thoracic cavity. The diagnosis is frequently missed, and the patient is liable to the hazard of strangulation of the herniated viscera. This carries a high mortality and may occur even 20 years after the original injury.

In the series of Probert and Havard (1961) the greatest incidence was from road traffic accidents, and the incidence of this cause of injury may be expected to rise.

The clinical features, in the *acute* phase, are of chest pain, dyspnea, tachycardia, shock, and cyanosis thus mimicking pneumothorax. Often the

diaphragmatic rupture is only one of several injuries, the most common being a ruptured spleen and fractures of the ribs and pelvis, and these concomitant injuries mainly determine the prognosis.

A second group of patients present in the *chronic* phase with complaints of dyspepsia, vomiting, chest pain, and a history of some previous injury.

A third group of patients present in the *late acute phase* with strangulation of the diaphragmatic hernia and the picture of acute intestinal obstruction, its severity depending upon involvement of small or large bowel. This is usually followed closely by acute cardiac and respiratory distress and may be associated with mediastinal shift away from the affected side. This type is associated with a high mortality.

Carter and Giuseffi (1948) reported that 90 per cent of strangulated diaphragmatic hernias were traumatic in origin. The site of the diaphragmatic tear is most commonly the left leaf. The mechanism whereby closed abdominal and chest injuries cause rupture of the diaphragm remains obscure. Car safety belts strapped across the abdomen might be expected to cause an increased incidence of ruptured diaphragm in car crashes but Garrett and Braunstein (1962), in a review of over 3,300 persons involved in car accidents when wearing belts did not find a single case of ruptured diaphragm.

The most useful diagnostic aid at any stage is a plain chest roentgenogram. The appearance has frequently been misinterpreted having been described as elevation of the hemidiaphragm, obliteration of the costophrenic angle, lower lobe collapse, pneumothorax of the lower chest, and volvulus of the stomach. In particular, the appearance of the distended wall of the stomach or colon may easily be interpreted as elevation or eventration of the diaphragm. A barium meal or enema examination may be useful to show the relations of the viscera in the hernia. Pneumoperitoneum is not recommended.

The most important factor in making a prompt diagnosis of rupture of the diaphragm is a suspicion of its presence; a chest roentgenogram is recommended for all patients who have sustained blunt abdominal injuries. This should be mandatory in those who have a fracture of the pelvis or ruptured spleen. The roentgenographic changes associated with the diaphragmatic hernia may not be immediately apparent, and a second roentgenogram should be made later if the patient complains of chest or abdominal pain.

Surgical repair of the diaphragmatic tear should be carried out as soon as the diagnosis has been established regardless of the stage at which the patient presents. Before surgery, it is most important to pass a gastric tube in order to lessen the risk of aspiration of stomach contents or cardiac arrest during induction of anesthesia.—*James R. Knapp, M.D.*

ABDOMEN

WEBB, DALE I., CHODOS, ROBERT B., HAHAR, CONSTANCE Q., and FALOON, WILLIAM W. Mechanism of vitamin B_{12} malabsorption in patients receiving colchicine. *New England J. Med.*, Oct. 17, 1968, *279*, 845–850. (From: The Department of Medicine, State University Hospital, Upstate Medical Center, State University of New York, and the Radioisotope Service, Veterans Administration Hospital, Syracuse, N. Y.)

The observation has been made that vitamin B_{12} absorption is reduced by colchicine administration.

Twenty patients were studied in an attempt to elucidate the mechanism of malabsorption. Schilling tests were done in all patients, and urine and fecal Co^{57} were measured during control and colchicine administration periods. This demonstrated significantly reduced vitamin B_{12} absorption in all but 1 patient.

Since diarrhea occurred in almost all patients given colchicine, similar studies were carried out using cascara to induce diarrhea; the fecal excretion was elevated but the urinary excretion was unchanged, indicating no effect on absorption by the diarrhea.

The possibility that gastric injury induced by colchicine was responsible for the vitamin B_{12} malabsorption was ruled out by preservation of normal intrinsic factor activity as measured in patients with pernicious anemia; gastric biopsies also revealed normal mucosa. The colchicine-induced vitamin B_{12} malabsorption was most profound when the colchicine was administered by tube into the ileum, indicating that the effect of colchicine is primarily upon the ileal site of absorption.—*Mark D. Reiss, M.D.*

GROTH, CARL G., BROWN, DONALD W., CLEAVELAND, JAMES D., CORDES, DAVID J., BRETTSCHNEIDER, LAWRENCE, and STARZL, THOMAS E. Radioisotope scanning in experimental and clinical orthotopic liver transplantation. *Surg., Gynec. & Obst.*, Oct., 1968, *279*, 808–816. (From: The Department of Surgery and the Division of Nuclear Medicine, University of Colorado School of Medicine, and Veterans Administration Hospital, Denver, Colo.)

Liver scannings performed with a rectilinear scintiscanner using technetium 99m sulfide colloidal suspension provide crucial and incisive information concerning organ size and functions in the

care of patients after orthotopic hepatic transplantation. Localized intrahepatic lesions such as abscesses and infarcts can be accurately identified and followed, using this method. The technique is described in detail.

Serial liver scannings were performed on dogs and humans. The scan findings were correlated with the serum bilirubin, alkaline phosphatase, serum glutamic oxalacetic transaminase, and serum glutamic pyruvic transaminase tests, as well as other clinical tests, plus autopsy studies when possible.

In 3 normal dogs, no changes were noted in liver function or in the appearance of the liver scans throughout the experiment; and at autopsy, the livers were grossly normal. In 2 dogs, upon whom a common bile duct ligation was performed, the liver scan remained normal except for the appearance of a large anterocentral defect which was shown at autopsy to be due to distention of the gallbladder. Biliary cirrhosis of the liver was also noted at autopsy. The hepatic artery was ligated in 3 dogs, and the liver scans were unchanged from the preoperative normal appearance throughout the 1 to 3 month period of study. At autopsy, the livers appeared to be grossly normal. An Eck fistula was constructed in 3 dogs, and the serial liver scans showed a definite and progressive diminution of liver size and development of areas of diminished radioisotope uptake. The diagnosis of hepatic atrophy was made at autopsy. Five dogs had an orthotopic hepatic homotransplantation and they received no immunosuppressive therapy. Two of the dogs died of hepatic artery thrombosis, and their scans were normal and unchanged from that demonstrated preoperatively in the donor. The other 3 dogs were considered on the basis of liver function tests and autopsy findings to have died of rejection. The liver scans in these cases showed a progressive loss of the magnitude and homogeneity of the radioisotope uptake.

Seven dogs had orthotopic hepatic homotransplantation with immunosuppressive therapy. In this group re-anesthetization every 1 to 3 days was poorly tolerated and the maximum survival was only 23 days. Three dogs that died before rejection had developed, had normal postoperative liver scans. Two dogs which lived for at least 1 week and showed evidence of rejection at autopsy had normal scans throughout life. The 2 other dogs which lived more than 1 week and died of rejection, showed scans which were similar to those in the untreated dogs undergoing graft rejection, including a reduction in the uniformity and density of the hepatic isotope configuration.

Scans were obtained in 3 other dogs, which had good liver function 16, 40, and 42 months after receiving orthotopic homografts. One of these dogs revealed a mild pattern of rejection, the other 2 showed an excellent and homogeneous isotope uptake, although their chronically tolerated homografts were smaller than normal dog livers.

Six infants, 1 with hepatoma and 5 with extrahepatic atresia, ages 14 to 24 months, received orthotopic liver homografts from cadaveric donors after removal of their own diseased livers. Three of these patients developed localized defects in the liver scans as well as an almost identical clinical syndrome. Each of the homografts was surgically explored; necrotic tracts were found within the liver and they were debrided and drained. One of these patients with liver infarction died within 1 week. In the other 2 patients, hepatic regeneration contributed to an eventual filling in of the defects.

In 1 of the patients without infarction, the liver scan remained normal without clinical evidence of rejection. Another patient without infarction developed a severe and protracted rejection 1 week after transplantation, and the scan showed a marked increase in size of the transplanted organ, while the isotope uptake was excellent. In 2 infants, 3 or more months after transplantation, the liver scan revealed a progressive shrinkage of the homografts and there was a decreased avidity for the isotope. In 1 of these cases, autopsy revealed advanced cirrhosis of the left hepatic lobe. The right lobe was previously infarcted.

The technetium 99m sulfide colloidal liver scan, because of the short half-life of technetium 99m and the low radiation dose of 1 rad per examination, is an excellent technique for the serial study of patients following orthotopic liver transplantation. The technique has proved to be valuable for diagnosing and localizing hepatic infarcts, following the course of hepatic regeneration, and estimating the effect of acute and chronic homograft rejection upon liver and Kupffer cell function.—*William T. McLaughlin, M.D.*

PAYNE, R. F. Drip infusion cholangiography. *Clin. Radiol.*, July, 1968, *19*, 291–295. (From: The X-ray Department, Bristol Royal Infirmary, Bristol 2, England.)

In this study 25 patients were investigated with drip infusion cholangiography. After a preliminary survey it was decided to infuse 250 ml. of 30 per cent dextrose with 60 ml. of Biligrafin Forte during 1 hour, since this large volume of contrast medium given over a relatively long time had caused no hypotensive effect. Films were exposed at ½ hourly intervals up to 3 hours. The roentgenograms were reviewed for the following features: (1) demonstration of the common bile duct: (2) demonstration of the gallbladder; (3) flow of contrast medium into the duodenum; (4) renal excretion; and (5) abnormal features.

The common bile duct was outlined in 23 of the 25 patients. The best demonstration of the duct occurred at 30 minutes. The best demonstration of the gallbladder was obtained at 2½ to 3 hours. Often these later roentgenograms demonstrated both the

duct and gallbladder together. Although the total amount of contrast medium is increased when compared to the standard injection, the dose rate per minute is less, resulting in less contrast medium being excreted by the kidneys. Should a severe reaction occur, an intravenous neddle is already in place. In this series no serious reactions occurred.—*Douglas S. Kellogg, M.D.*

Turner, F. W., and Costopoulos, L. B. Percutaneous transhepatic cholangiography: a study of 115 cases. *Canad. M. A. J.*, Sept. 21, 1968, *99*, 513–521. (Address: Dr. F. W. Turner, Clinical Instructor in Surgery, University of Alberta, University Hospital, Edmonton, Alberta, Canada.)

A report is made of 115 cases in which percutaneous transhepatic cholangiography was attempted in both jaundiced and nonjaundiced patients. There are 2 indications for performing percutaneous transhepatic cholangiography: (1) to determine the cause and site of extrahepatic biliary obstruction, and (2) to distinguish between obstructive and nonobstructive jaundice. Encompassed within the first of these is the expectation of defining accurately; (a) the presence and location of a biliary calculus or of calculi and possibly their number; (b) the presence and site of neoplasma of the major bile ducts, of the ampulla of Vater and/or of the head of the pancreas; and (c) the position and degree of both benign and malignant strictures of the major bile ducts.

In the 115 cases of attempted percutaneous transhepatic cholangiography there have been 8 complications. On 5 occasions the operating surgeon described the presence of large amounts of bile-stained fluid in the peritoneal cavity. All of these patients had extrahepatic biliary obstruction. After their initial experience with this problem, laparotomy was insisted upon as soon as possible in all patients shown to have obstruction of the extrahepatic bile ducts. As a result, bile leakage did not present any additional problem in the other 4 patients. The presence of subcapsular hematoma of the liver was noted on 2 occasions. These were evacuated at the time of operation without initiating any fresh bleeding. In neither case did the estimated blood loss exceed 200 cc. In 1 patient a postoperative chest roentgenogram demonstrated a small pneumothorax which was attributed to the cholangiography. It did not require treatment.

Thirty-four patients had either solitary or multiple stones in the extrahepatic ductal system. Mobile stones appeared as radiolucent filling defects surrounded by contrast medium. Larger impacted stones were covered with contrast medium only on their superior surface and gave a characteristic "cupping" configuration.

Of 23 patients with carcinoma of the head of the pancreas, the majority showed the characteristic triad: a greatly dilated common bile duct, a rounded configuration of the distal end of the common bile duct and complete obstruction to the flow of contrast medium. In 7 patients with carcinoma of the ampulla of Vater the typical changes were either an uneven margin at the site of obstruction or a conical configuration.

The common bile duct lesions included: (1) 8 benign ductal strictures; (2) 3 patients with carcinoma of the common bile duct; (3) metastatic lesions; and (4) 3 patients with carcinoma of the gallbladder showed secondary involvement of the common duct producing considerable stenosis.

It is concluded from this study that percutaneous transhepatic cholangiography performed with due care and with close cooperation between the surgeon and radiologist in selected patients with jaundice, the cause of which cannot be elucidated by other means, is a safe and valuable diagnostic procedure.—*Douglas S. Kellogg, M.D.*

Tréheux, A., Fays, J., Crestin, M., and Heully, F. Intérêt de la cholangiographie intraveineuse et de la duodenographie simultanées dans l'étude de l'ampoule de Vater et des pancréatites chroniques. (Nancy, France.) (The significance of intravenous cholangiography associated with duodenography in the study of the ampulla of Vater and chronic pancreatitis.) *J. de radiol., d'électrol. et de méd. nucléaire*, June-July, 1968, *49*, 471-476.

The authors visualize sumultaneously the biliary ducts by means of cholangiography and the duodenum by catheterization duodenography. Twenty minutes after intravenous injection of an anticholinergic substance, the duodenum is catheterized and 40 cc. of Xylocaine is instilled into it. Thus, hypotonicity of the duodenal loop is obtained, and then a barium suspension is instilled and duodenography performed. Various roentgenograms are taken in the supine and oblique positions. The barium is withdrawn through the catheter and, instead, air is injected into the duodenum for air contrast views, and thus finer details of the mucosal pattern are visualized.

Thirty normal patients were examined in this manner in order to determine the normal roentgenographic images in the region of the ampulla of Vater. Twenty-five cases presenting gastroduodenal abnormalities as well as biliary pathology were also examined. It is easy to demonstrate abnormality of the ampulla of Vater; however, it is difficult to determine the cause of the abnormality. Thus, an ampulla of Vater is abnormal when its size is increased and its contour irregular. The irregularity sometimes extends to the distal end of the common duct. Thus, it would be difficult to differentiate

between inflammatory condition of the ampulla of Vater and that of the pancreatic duct and neoplastic changes in this region. However, usually, neoplastic processes are accompanied by obstructive jaundice. In case of jaundice, roentgenographic examination is contraindicated. Chronic pancreatitis would cause narrowing of the ampulla of Vater and of the distal 1 or 2 cm. of the common bile duct to the extent that there is dilatation of the latter duct proximally. Certain roentgen alterations point to hypertrophy of the sphincter. Diverticulum of paravaterian region has been demonstrated. In chronic pancreatitis, certain changes can be noted along the duodenum and, at times, other changes can be noted along the common bile duct. Such changes are irregularity of the inner lining of the duodenum at the region of the ampulla of Vater and slight retraction of the duodenum parallel to the intrapancreatic portion of the common duct and pancreatic calcification. It is also possible to differentiate this calcification from a pancreatic duct calculus, as this latter is usually ovoid and smooth as to its contour, with its long axis parallel to the distal end of the common bile duct. Slight irregularity of the duodenum close to the ampulla of Vater could be of significance when examined in the light of any compression of the pancreatic portion of the common bile duct. On the other hand, at times, the distal end of the common bile duct is not narrowed and is not compressed; however, there is a co-existent alteration, or irregularity, of the mucosal lining of the duodenum in the vicinity of ampulla of Vater which signifies pancreatitis. Also, it is important to know that in chronic pancreatitis, most of the time, the ampulla of Vater, itself, has a normal configuration. Finally, in certain cases, it has been possible to rule out, definitely, a suspected diagnosis of pancreatitis on the basis of this simultaneous examination of the duodenum and of the common bile duct.—*Jirair N. Sarian, M.D.*

GYNECOLOGY AND OBSTETRICS

GROS, CH., WALTER, J. P., and DELLENBACH, P. Le diagnostic radiologique de la mort foetale. (Strasbourg, France.) (Radiologic diagnosis of fetal death.) *J. de radiol., d'électrol. et de méd. nucléaire*, Aug.-Sept., 1968, *49*, 562–565.

The authors do not share in the common pessimism regarding radiologic diagnosis of fetal death, since they made correct determinations 80 per cent of the time.

They found intrafetal gas in 30 per cent of their 30 cases, of which 6 were demonstrated within 48 hours of fetal death, and 1 at 6 hours. The halo sign, due to edema of tissues beneath the scalp, occurs in from 70 to 90 per cent of cases, but is hard to demonstrate, so that a cone view over the fetal head is indispensable. The radiolucent space exceeds 3 mm. in width by 24 hours after fetal death, becoming progressively wider.

Amniography has at least 3 advantages: (1) it facilitates recognition of the halo sign; (2) fetal malformations may be identifiable; and (3) it can produce a positive sign of fetal life, by the demonstration of fetal deglutition, and resultant visualization of intestinal loops. Amniography should always be done when intrauterine transfusion is planned. In one spectacular case of the authors, fetal death in one twin and life in the other were revealed by amniography.—*Frank A. Riebel, M.D.*

KATTAN, KENNETH R., and SPITZ, HAROLD B. Roentgen findings in obstetrical injuries to the brachial plexus. *Radiology*, Sept., 1968, *91*, 462–466. (From: The Department of Radiology, University of Cincinnati, Cincinnati General Hospital, Cincinnati, Ohio 45229.)

The roentgen findings in obstetrical injuries to the brachial plexus in the newborn are: increased distance between glenoid cavity and humeral metaphysis, retarded development of the humeral head epiphysis, elevation and outward rotation of the scapula, soft tissue atrophy, and elevation of the diaphragm on the involved side if the phrenic nerve is involved.

The roentgen findings in the older child and adult are: increased outward rotation and elevation of the scapula, increased internal rotation and subluxation of the humeral head from the glenoid fossa, elongated acromion, and a delayed development of the elbow with small epiphysis. There may also be an underdevelopment of the clavicle or a small and flattened glenoid.

The roentgen findings are due to an increased pressure on the brachial plexus as a result of separation of the infant's head and neck at delivery. This may cause temporary or permanent paralysis of the muscles of the involved shoulder and arm. The upper arm type, Erb's paralysis, is caused by injury to the 5th and 6th cervical nerve roots. The uncommon lower arm type, Klumpke's paralysis, is caused by injury to the 7th and 8th cervical and 1st thoracic nerve roots.

Clinically, the arm hangs at the side pronated and in internal rotation with the elbow and wrist flexed, the "waiter's tip" position. If paralysis persists, the limb becomes atrophic, and contractures develop If the cervical sympathetic fibers are injured, a Horner's syndrome develops.—*C. T. Edmondson, M.D.*

GENITOURINARY SYSTEM

NEMOY, NORMAN J., and FORSBERG, LEIGH. Polycystic renal disease presenting as medullary sponge kidney. *J. Urol.*, Oct., 1968, *100*,

407–411. (From: The Division of Urology and the Division of Diagnostic Radiology, Palo Alto Veterans Administration Hospital, Palo Alto, Calif.)

The authors report a single well investigated and thoroughly studied white man who on intravenous and retrograde pyelography had evidence of multiple small cystic defects involving the renal pyramids associated with small urinary calculi and incidental *Pseudomonas* infection.

At operation the lower pole of the left kidney was removed because of infection. The resected specimen showed multiple cortical cysts and the histologic examination revealed cortical and medullary cysts. The pyelogram did not demonstrate the usual changes of stretched pelvicalyceal system, and the patient did not exhibit hypertension or diminished renal function. Both kidneys were noted to be somewhat enlarged.

This is one of the few reported cases in which medullary sponge kidney was associated with polycystic disease. The question of whether medullary sponge kidney is a distinct entity is not answered. It is suggested that polycystic renal disease may be the basic pathology when roentgenographic evidence of medullary sponge kidney is associated with enlarged kidneys.

The authors include 5 figures and 2 tables which illustrate the gross roentgenographic and histologic findings.—*George W. Chamberlin, M.D.*

BECKER, JOSHUA A., WEISS, ROBERT M., and LATTIMER, JOHN K. Renal tuberculosis: role of nephrotomography and angiography. *J. Urol.*, Oct., 1968, *100*, 415–419. (From: The Department of Radiology and the Research Unit for Genito-Urinary Tuberculosis, Columbia-Presbyterian Medical Center, New York, N. Y.)

This is a report based upon 27 cases of renal tuberculosis proven by culture. All patients were studied by drip infusion nephrotomographic technique and 7 patients had selective renal arteriography.

The authors found that neither tomography nor angiography aided in the roentgenographic diagnosis of renal tuberculosis in those instances in which the excretory urogram was normal or minimally abnormal. When gross abnormalities such as stricture formations were present, the nephrotomograms demonstrated the remaining renal substance and angiography confirmed the findings of the tomography.

Arteriography offered no additional information in the diagnosis of an advanced case of renal tuberculosis and therefore does not seem to be indicated in the routine evaluation of patients with renal tuberculosis.

The roentgenographic findings did not influence the therapy of the patients with renal tuberculosis.

The authors present 5 composite illustrations of the pyelograms of some of the patients in this study.—*George W. Chamberlin, M.D.*

BRIJS, A. Extravasate bei intravenöser Urographie. (Extravasates with intravenous urography.) *Fortschr. a. d. Geb. d. Röntgenstrahlen u. d. Nuklearmedizin*, Sept., 1968, *109*, 375–380. (Address: Dr. A. Brijs, Ste. Elisabethgasthuis, Abt. Radiologie, Nederrij, 137, Herentals, Belgium.)

Extravasations of contrast material are occasionally observed during retrograde pyelography, but as a result of intravenous urography they are considered rare. Only 32 such instances have been recorded in the literature prior to 1960. The author now reports 2 well documented cases.

The first patient, a 46 year old man, was admitted to the hospital because of a renal colic. Urography revealed satisfactory excretion of both kidneys; however, there was caliectasis with incomplete filling of the left kidney pelvis and nonfilling of the left ureter even at a late phase. Gradually, contrast material appeared in the left pericalyceal and peripelvic area and alongside the left upper ureter. An exploratory operation at this time failed to disclose abnormal findings. Sixteen days later, repeated urography revealed a perfectly normal condition.

The second patient, a 58 year old woman, was admitted to the hospital with the tentative diagnosis of an incarcerated left inguinal hernia. The right kidney had been removed 20 years previously. Urography revealed good excretion of the left kidney, but dilatation of its collecting system. A small calculus was observed in the left lower ureter at the ureterovesical junction. Fifteen minutes following the injection of contrast material, a pericalyceal extravasate appeared at the lower pole of the left kidney, spreading gradually to the retroperitoneal space alongside the left upper ureter. The condition required no radical measures and the symptoms subsided with the aid of medical management.

Small rents in a minor calyx, as observed in both patients, tend to seal off spontaneously. The therapy must be conservative and directed toward lowering the increased pressure within the collecting system. Abdominal compression aggravates this pressure and has to be avoided. Surgical measures are also contraindicated and superfluous in most instances. Pyelovenous, pyelotubular and pyelolymphatic reflux and extravasates occur almost exclusively during retrograde pyelography and, therefore, offer

no problems of differential diagnosis.—*Ernest Kraft, M.D.*

MAXWELL, MORTON H., and LUPU, ANDREI N. Excretory urogram in renal arterial hypertension. *J. Urol.*, Oct., 1968, *100*, 395–406. (From: The Renal Hypertension Service, Cedars-Sinai Medical Center; the Cedars-Sinai Medical Research Institute and the Departments of Medicine and Surgery, UCLA Medical Center, Los Angeles, Calif.)

In this article the authors have used reports from the literature to evaluate the excretory urogram in patients who have hypertension. In the final analysis, this evaluation is directed toward patients who have unilateral or bilateral renal artery stenosis and diastolic hypertension. It is pointed out that renal artery stenosis may be present in the absence of hypertension; and, therefore, renal artery stenosis hypertension may be an incidental finding and unrelated to the diastolic pressure.

The parameters which have been used in the study of the excretory urogram are: (1) kidney size as measured by the length of the renal parenchymal shadow on the urogram; (2) pyelocalyceal appearance time as measured by rapid sequence urography at 1 minute intervals for 5 minutes; (3) the relative density of the early nephrogram phase on the excretory urogram; (4) pyelo-calyceal concentration as seen on the dehydrated urogram; (5) calyceal concentration and nephrogram as noted on the urea infusion urogram; (6) pyelocalyceal spasticity; (7) nonfunctioning kidney on the urogram; and (8) ureteral notching as seen on the urogram. Each one of these parameters is discussed in detail, and its individual diagnostic and prognostic value is considered.

The authors state that in the past many of those who have studied this problem have considered the intravenous urogram as misleading or of no value in the determination of functional disturbances. In this article they show that with newer methods, careful attention to the various criteria and with modification of the excretory urogram, much valuable information is obtained. At the same time, other types of renal disorders, whether pertaining to hypertension or not, are also evaluated by proper excretory urograms.

Urography is widely available and relatively safe compared to other methods for determining renal arterial hypertension. In a large number of patients with essential hypertension, the incidence of falsely positive results was less than 10 per cent.

When one evaluates only those articles from the literature in which the cases presented have had proven renal artery stenosis, when adequate criteria were evaluated and when definite findings of positive and negative results were reported, it is apparent that the combination of an unsuggestive clinical picture and a normal appearance time on the rapid sequence study is sufficient to eliminate unilateral renal disease as a cause of hypertension. In other words, a properly conducted excretory urography, if negative for evidence of renal hypertension, is a good screening procedure.

At the present time, further information with regards to some of the parameters previously mentioned is necessary to completely evaluate the diagnostic and prognostic limitations and advantages of excretory urography in renal arterial hypertension. The newer modifications of techniques have improved the sensitivity and specificity of this procedure for screening purposes.—*George W. Chamberlin, M.D.*

WINTER, CHESTER C., ELLIOTT, JOHN, GRACE, DONALD, and ROBERTSON, ALEX. Radioisotope renography in assessment of renal function in newborn. *J. Urol.*, Aug., 1968, *100*, 99–103. (From: The Departments of Surgery and Pediatrics, Ohio State University College of Medicine, Columbus, Ohio.)

The authors report on experience with radioisotope renography in using I^{125} (o-iodo-hippurate) in 26 apparently normal newborn infants ranging in age from 25 to 95 hours.

Two scintillation counters with crystals 0.5 inch in diameter and 2 mm. thick were placed under the kidneys. A dual, overlapping, pen recorder was connected with the probes through 2 rate meters.

Random urine samples for microscopic examination and osmolality determinations were collected for correlation. More precise measurements of renal function such as creatinine and urea nitrogen, etc. were not attempted.

Nineteen of the 26 subjects were judged to be normal. *Tm*, the time from injection to maximum renal radioactivity, averaged 2.8 minutes with a range of 1.8 to 4.5 minutes in these subjects. $T\frac{1}{2}$, time interval from injection until renal radioactivity returned halfway to the base line from its peak activity, averaged 11.5 minutes with a range of 7.8 to 21.0 minutes in these normals.

The abnormal tracings generally showed prolonged functional and/or excretory pattern.

The authors discuss the advantages and disadvantages of I^{125} compared to I^{131} and suggest that this test is perhaps better as an initial survey procedure than the excretory urogram because of the much lower radiation dose received. They suggest further that if a normal renogram is found, no additional renal tests should be necessary, whereas an abnormal renogram would indicate the need for more specific tests.—*George W. Chamberlin, M.D.*

Figueroa, Julio E., Maxfield, William S., Batson, Hugh M., and Birchall, Robert. Radioisotope renal function studies in human renal allografts: value in differential diagnosis of oliguria in presence of obstructive disease with and without urinary extravasation. *J. Urol.*, Aug., 1968, *100*, 104–108. (From: The Departments of Internal Medicine and Radiation Therapy, Ochsner Clinic and the Biophysics Laboratory, Ochsner Foundation Hospital, New Orleans, La.)

The authors report on their experience with a combination of renographic and serial scintillation scanning studies, using radiohippuran in 8 patients who had had renal transplants. The case reports of 3 of these patients are presented.

The authors feel that with these combined studies, one can differentiate diminished function due to obstruction with or without urinary extravasation from those cases in which the functional decrease is the result of an intrarenal cause or rejection. They favor hippuran over radiomercury because of the ability to detect urinary extravasation with hippuran due to its rapid flushing from the kidney. The ability to do series studies with hippuran is also cited as an advantage over mercury.—*George W. Chamberlin, M.D.*

Brooks, V., and Bateson, E. M. Cysto-urethrography in the University Hospital of the West Indies. *Clin. Radiol.*, July, 1968, *19*, 278–286. (From: The Departments of Surgery and Radiology, University Hospital, Mona, Kingston 7, Jamaica, West Indies.)

Cysto-urethrography was performed on 100 patients with complicated urethral stricture, and the findings were correlated at operation.

The indications for cysto-urethrography and surgery were as follows: (1) impassable stricture; (2) strictures requiring frequent dilatations; (3) in those cases where dilatation had been followed by septicemia or other septic complication; and (4) in presence of periurethral sepsis and/or fistulae.

A study of these 100 urethrographies revealed the presence of stricture in 97 patients. In the remaining 3 patients, fistulous tracts were demonstrated but no definite stricture could be identified by cysto-urethrography. The importance of both ascending and micturating cysto-urethrograms is stressed. The descending cysto-urethrogram is of special value in illustrating the dynamic aspects of the pathologic changes. In particular, the descent and opening of the bladder neck, the dilatation of the urethra proximal to the stricture, the filling of diseased prostatic ducts, abscesses and seminal vesicles, the distention of urethral diverticula and the escape of contrast material through the fistulous tracts are all best visualized on roentgenograms taken during micturition. The ascending roentgenograms are of particular value in demonstrating the caliber of the urethra distal to the site of obstruction.

In the present series most of the strictures were inflammatory in origin. The high incidence of complications, especially fistulae, is thought to result from the initial treatment of stricture by repeated bouginage with secondary infection.—*Douglas S. Kellogg, M.D.*

Bandtlow, K. Urethrozystographie. (Urethrocystography.) *Röntgen Blätter*, 1968, *21*, 434–443. (Address: Dr. K. Bandtlow, Chir. Univ.-Klinik, Urologische Abteilung, Anichstr. 35, 6020 Innsbruck, Austria.)

Urethrocystography (UCG) has been described almost 60 years ago, but only in recent years has it become more widely accepted. Improved contrast media and refined roentgenographic equipment have aided in making the method more popular. The author now reports his experience with 5,700 examinations he has performed during the past 10 years.

UCG can be done either as a voiding or retrograde procedure. Both methods yield varying information and thereby complement each other. For the voiding UCG, a solution containing 20 parts of 76 per cent urografin and 80 parts of a saline solution is used. For the retrograde UCG, the urografin is mixed with an equal amount of a high-viscosity solution containing cellulose.

Roentgenograms are made in the right oblique projection, with the perpendicular beam centered over the pubic symphysis, while the right hip and right knee are held in 90° flexion. For the voiding UCG, erect views are preferable. For the retrograde UCG, exposures are made at the end of 2 injections of 10 cc. each, of the high-viscosity solution. An anesthetic contained in this mixture minimizes accompanying pain. The injection must not be forced, otherwise mucosal rents and venous reflux are bound to develop. Oily solutions and barium mixtures can be harmful and must be avoided. UCG is also contraindicated in acute urethritis and following cystoscopy and bouginage.

The various indications and results are discussed together with pertinent illustrations. In stenosis, a prestenotic dilatation can be demonstrated with the retrograde as well as the voiding UCG, and both methods are recommended for complete information. In prostatectomies, residual tissue following electroresection is well shown. Periurethral edema following bouginage of a stenosis presents with wavy and unsharp contours of the urethra. When calcifications are present, a tuberculous urethritis has to be suspected.

Injuries are best demonstrated with the retrograde method, while for malformations with vesicoureteral reflux and for fistulas the voiding urethrogram is decisive. Obstruction of the bladder neck due to prostatic enlargement is one of the most common findings. Extrinsic pressure bilaterally causes a swordblade flattening, while anterior curving of the urethra is characteristic of prostatic carcinoma. When the cancer perforates into the lumen, an irregular contour results. So-called sphincter sclerosis with stenotic narrowing of the urethral lumen can be well differentiated from prostatic adenoma. In this condition, a rigidity prevents contraction of the bladder neck even during voiding so that the usual funnel formation is absent. Another indication for UCG is a routine caliber testing prior to endoscopic procedures.

UCG deserves wide application as the results are most revealing especially in unrecognized injuries and malformations. Complications are quite rare when the instruments are carefully sterilized, modern contrast media are used and the injections made cautiously.—*Ernest Kraft, M.D.*

SKELETAL SYSTEM

CARROLL, T. B., and GRUBER, F. H. Seat belt fractures: a report of two cases. *Radiology*, Sept., 1968, *91*, 517–518. (Address: Dr. F. H. Gruber, Medical College of South Carolina, Charleston, S. C. 29407.)

Two case reports of fractures of the lumbar spine secondary to improperly placed seat belts are presented and the previous literature is reviewed. The mechanism of production is discussed, with the concept of flexion of the spine superior to the fixed, confining seat belt being indicted.

The characteristic features of the fractures are:

1. Involvement of one or more of the upper lumbar vertebrae;

2. transverse fracture involving the posterior aspect of the vertebra—through the spinous process, lamina, pedicles, and into the posterior body and transverse processes;

3. separation posteriorly of the fragments without subluxation of the vertebral bodies;

4. large associated hematoma over the fracture site; and

5. no neurologic deficit in any of the 5 previously reported cases although there was a persistent weakness in 1 of the currently reported ones.—*John P. Eberts, M.D.*

FRIEDENBERG, Z. B., and KOHANIM, M. The effect of direct current on bone. *Surg., Gynec. & Obst.*, July, 1968, *127*, 97–102. (From: The Department of Orthopedic Surgery, Hospital of the University of Pennsylvania and School of Medicine University of Pennsylvania, Philadelphia, Pa.)

The authors report the results of an investigation to determine if bone growth in 52 five to eight week old white New Zealand rabbits could be influenced by a physiologic range of 3 to 10 microamperes current. In one group of rabbits the current flowing across the tibial epiphyseal cartilage was studied and in another group the current effect on a local segment of tibial metaphyseal diaphyseal bone was analyzed. For each group control rabbits were utilized for comparison. The animals were sacrificed and the length of the tibias was measured with calipers. Roentgenograms of the experimental and control excised tibias were made on high speed industrial film, Type R, at a distance of 39 cm. and compared for length and developmental changes. Microscopic pathologic studies were also carried out. Forty of the 52 rabbits were included in the compilation of the results, the other 12 being excluded because of failure of the electric current or infection.

The rabbits were divided into 4 groups based on current days. No significant increase in tibial length in any group was noted. Roentgenograms of the groups receiving current across the epiphyseal bone showed a high incidence of bone destruction surrounding the positive pole in the metaphysis; and radiolucency surrounding the wire (12/17 rabbits). No destructive changes were noted adjacent to the negative terminal in any rabbit, whether the terminal was epiphyseal or metaphyseal. The roentgenologic findings of the groups receiving current between the metaphysis and the diaphysis were similar for the positive electrode. The microscopic pathologic studies were corroborative and showed a minimal amount of connective tissue, cartilage, and bone developing in relation to the negative pole in some rabbits.

The observations in this report strongly suggest that with minimal currents in a physiologic range the positive pole selectively destroys tissue.—*Lionel W. Young, M.D.*

ALLEN, E. H., MILLARD, F. J. C., and NASSIM, J. R. Hypo-hyperparathyroidism. *Arch. Dis. Childhood*, June, 1968, *43*, 295–301. (Address: Dr. F. J. C. Millard, St George's Hospital, S.W.1, London, England.)

The authors report the chemical findings of hypoparathyroidism and the roentgenologic findings of hyperparathyroidism in a 10 year old boy who recovered following dihydrotachysterol administration. In 1963, Costello and Dent described a similar patient.

The roentgenologic findings are: metaphyseal irregularity and density, epiphyseal plate widening, phalangeal and radial cortical erosions, cystic areas

in several tubular bones, widened costochondral junctions, dorsal and lumbar vertebrae showing alternating bands of increased and decreased density and irregularities of the distal ends of the clavicles. The diagnosis of hyperparathyroidism rests on the roentgen changes.

The authors suggest that, based on the response to moderate doses of vitamin D therapy in the reported patients, this hyperparathyroidism may be secondary, although no condition likely to cause secondary hyperparathyroidism was found in either patient.

The bone biopsy finding of an excess of osteoid suggests the possibility of some unusual form of rickets with hyperparathyroidism secondary. However, roentgenologic appearance of the metaphyses is not typical of rickets although superficially resembles it. It has been suggested that the increased metaphyseal density in some patients with hyperparathyroidism is due to excess calcitonin.

The authors conclude that they can find no satisfactory alternative to the attractive theory of simultaneous development of hypo-hyperparathyroidism. One postulation is that the parathyroid secretes two hormones, one that raises the serum calcium and lowers the phosphorus and another that causes osteitis fibrosa and raises the alkaline phosphatase.—*Lionel W. Young, M.D.*

BOSTRÖM, H., EDGREN, B., NILSONNE, U., and WESTER, P. O. Metabolic and orthopedic treatment of a case of adult nonfamiliar hypophosphatemia with severe osteomalacia. *Acta orthop. scandinav.*, 1968, *39*, 238–260. (From: The Departments of Medicine, Serafimerlasarettet, and Orthopedic Surgery Norrbacka Institutet, Karolinska Institutet, Stockholm, Sweden.)

A case of severe hypophosphatemic nonhereditary osteomalacia with renal glycosuria is described in a 27 year old man. The roentgenographic evidence of osteomalacia was very marked, with numerous pseudofractures in various stages, some with extensive callus formation. Typical vertebral changes were present, and in addition a vertebral fracture with marked gibbus complicated the picture. There was also a sternal fracture with pigeon-breast deformity. Synptoms of slowly progressive bone pain had been present for 10 years, but the very severe nature of his disease rapidly began to become manifest after a gastric resection for peptic ulcer at the age of 23 years. The patient had lost 16.5 cm. in body height, was severely crippled by the gibbus and pigeon-breast deformity, had constant skeletal pain, and was mentally depressed.

In addition to high doses of vitamin D and calcium the patient was given sodium monophosphate, prior treatment with vitamin D alone having been unsuccessful. By 4 weeks there was a notable decrease in pain; by 5 months marked increase in callus formation was seen; and by 7 months all the pseudofractures had completely healed. The dramatic improvement was seen in all parameters of his disease, and his mental depression disappeared. Concurrent with medical therapy, orthopedic treatment with spinal traction and plaster fixation was successful in adding 5.5 cm. to his height.

The metabolic balance studies for calcium, phosphorus, and a number of tracer elements before and during treatment are discussed. The effect of treatment on iron absorption, skeletal muscle function, and bone microradiography are also evaluated.

The experience from this case supports the view that oral phosphate has a place in the treatment of hypophosphatemic osteomalacia, and that orthopedic treatment has much to offer in severe cases of this disease.—*Mark D. Reiss, M.D.*

GALASKO, C. S. B., WESTERMAN, B., LI, J., SELLWOOD, R. A., and BURN, J. IAN. Use of the gamma camera for early detection of osseous metastases from mammary cancer. *Brit. J. Surg.*, Aug., 1968, *55*, 613–615. (From: Breast Clinic and Departments of Surgery, Medical Physics, and Diagnostic Radiology, Hammersmith Hospital and Royal Postgraduate School of Medicine, London, England.)

The skeleton is the most common site for metastases from mammary carcinoma, bone lesions being found at autopsy in 85 per cent of patients dying from the disease. Some 50 per cent of these lesions are not apparent on the roentgenograms. Radioisotopic scanning is reported to be more reliable than roentgenographic survey but takes from 6 to 8 hours and is too laborious for routine use. With the gamma camera, axial skeletal scintigraphy can be performed in 90 minutes and would seem to be an ideal choice for metastatic survey prior to treatment.

Eight patients with osseous metastases from breast cancer were studied with a gamma camera. Separate studies were made with fluorine 18 and with strontium 87m. With F^{18} all lesions visible on the roentgenograms were apparent on the scintigram, and additional metastatic lesions not roentgenographically visible were found in 6 of the 8 patients; in 4 of these, roentgenographic confirmation was obtained 3–4 months later. With Sr^{87m} some lesions were not demonstrated in 4 of the 8 patients, and additional lesions were found in 4 of the 8 patients. Fluorine 18 is clearly a more suitable isotope for the detection of osseous metastases than strontium 87m, but unfortunately the use of F^{18} must be limited, since it is manufactured in a cyclotron and has a

very short half-life, thus not being easily obtained in all centers.—*Mark D. Reiss, M.D.*

BLOOD AND LYMPH SYSTEM

DOTTER, CHARLES T., RÖSCH, JOSEF, and JUDKINS, MELVIN P. Transluminal dilatation of atherosclerotic stenosis. *Surg., Gynec. & Obst.*, Oct., 1968, *279*, 794–804. (From: The Stella and Charles Guttman Institute for Vascular Research through Radiology at the University of Oregon Medical School, Portland, Oreg.)

Non-operative, lasting clinically effective dilatation of uncomplicated atherosclerotic stenoses can be achieved by percutaneous catheter technique. The luminal narrowing due to a primary atherosclerotic lesion is relieved by remodeling it by means of forceful dilatation with a catheter. The atheroma is reduced in volume by squeezing the fat out of it. The method avoids surgical trauma and preserves the surface of arterial lining and the outer wall.

Patient selection is important. The ideal candidate is a patient whose arteriogram shows a sharply outlined localized narrowing of the distal portion of the superficial femoral artery. Complete occlusions cannot be treated by simple dilatation, but other methods are being developed.

Transluminal dilatation can avert otherwise necessary amputations and relieve the symptoms of ischemia of the lower extremities in patients generally regarded as unsuitable for operation because of poor runoff arteries or general physical debility.

The technique is described in detail. The facilities needed are those needed for selective percutaneous arterial catheterization. The operator should be experienced in the use of intra-arterial catheters. Skill and attention to technical detail will prevent the deformation of the tips of the dilatation catheters, mural separation at the site of entry, intimal plowing, and atheromatous dislodgement. The tip of the guidewire or the dilatation catheter should not be allowed to pass outside of the arterial lumen. Dilatation should not be carried out further distally than is necessary. After the dilatation, both catheters are withdrawn to a proximal point, and angiograms are made; then 5,000 U.S.P. units of heparin are injected, the catheters are removed, and manual hemostasis is achieved through digital point pressure directly over the site of the arterial puncture. The patient is allowed to walk the same day. Heparin is administered for the next 4 days, the dosage being adjusted to double the clotting time.

The authors review 155 consecutive patients; 119 patients, including 26 instances of occlusion of the superficial femoral artery, received treatment in the region of the femoral artery system. In 21, or 80 per cent, of these 26 patients, the procedure was judged successful. Ten out of the 11 most recent consecutive transluminal dilatations appear to have been successful. In the entire series of 155 patients, 1 death occurred as a direct or indirect result.

Eight cases are reported with serial angiograms demonstrating the therapeutic result obtained.

It is believed that transluminal dilatation is the primary treatment—the treatment of choice—for patients with ischemia of the lower extremity due to stenosis, single or multiple, localized or diffused, within the femoral popliteal artery system. Such patients are good candidates, however mild or severe their symptoms, whatever the condition of the runoff arteries, with or without gangrene, and regardless of whether conventional surgical intervention appears feasible or not

The over-all success rate of this new procedure has been 80 per cent and is improving.—*William T. Mc Laughlin, M.D.*

LEBOUCHARD, R., GILLOT, C., ROBERT, F. W., and CHICHE, P. Apport de la phlébographie occlusive dans le controle des anastomoses portocaves thérapeutiques. (Paris, France.) (The significance of occlusive phlebography in the evaluation of therapeutic portocaval anastomoses.) *J. de radiol., d'électrol. et de méd. nucléaire*, June-July, 1968, *49*, 445–450.

Occlusive phlebography is a recently developed method used in the opacification of various branches of the inferior vena cava. It is also called bi-occlusive cavography.

This is accomplished by inserting a catheter through the saphenous vein under general anesthesia and with very strict aseptic precautions. The catheter has 2 small balloons about 8 cm. apart, each with a small radiopaque indicator, to pin point their position. Once the end of this intravenous catheter reaches the desired level, then the balloons are inflated by injection of physiologic saline, thus occluding the inferior vena cava at 2 levels, 8 cm. apart. Into this space, between the inflated balloons, about 100 cc. of contrast solution is injected, within 10 to 15 seconds, under about 2 kg. pressure per square centimeter.

This examination will enable a thorough analysis of the condition of the renal veins, esepcially in case of nephrotic syndrome. Thus, 12 thromboses of the renal vein were demonstrated (out of 80 such instances). This examination is also very useful in evaluating therapeutic portocaval anastomoses and will give valuable information as to spontaneous portocaval shunts.

Exploration of portocaval therapeutic shunts by means of occlusive phlebography is very important, as such anastomoses are susceptible to thrombosis, especially at the splenorenal level (approximately 30 per cent, according to the authors).

This examination furthermore will reveal the

degree of patency of these anastomoses in the absence of any thrombosis.

The procedure is well tolerated. The possibility of arterial hypotension occurring approximately 4 hours after such an examination should be kept in mind, so as to control it effectively by neosynephrine.

Three periods can be considered in the exploration of the portocaval anastomoses. The first period is during the first 3 weeks. The second period is examination approximately 6 months later, and the third period of exploration could be as late as 5 years. In the early exploration, one is mainly concerned with postoperative complications. The renal factor is found to be important in these anastomoses.

Bi-occlusive cavography enables a detailed analysis of the afferent tributaries, of residual varices, and, to a certain extent, of the condition of the liver after therapeutic anastomoses.—*Jirair N. Sarian, M.D.*

Son, Yung H., Wetzel, Richard A., and Wilson, William J. ^{99m}Tc pertechnetate scintiphotography as diagnostic and follow-up aids in major vascular obstruction due to malignant neoplasm. *Radiology*, Aug., 1968, *91*, 349–357. (From: Department of Radiology, University of Virginia School of Medicine, Charlottesville, Va.)

Neoplastic obstruction of the superior vena cava is considered an emergency to be treated with radiotherapy. Neoplastic obstruction of the abdominal or pelvic vessels may be just as effectively treated although not necessarily on an emergency basis. Cytostatic agents and steroids may be adjunctive in obstructions of lymphomatous origin. Due to "inoperability" status surgery is infrequently used.

Plethora, choking, venous distention, cyanosis, and neck edema are common signs of superior vena cava obstruction. Venous pressure determinations, infra-red photography and angiography are confirmatory procedures. Routine roentgenograms seldom tell the whole story. The inherent morbidity and infrequent mortality of angiography and cavography limit their use.

Use of the gamma camera with rapid sequential imaging of the intravascular course of technetium (Tc^{99m}) pertechnetate boli presents a possible routine method of accurately determining the site and the extent of the obstructive phenomena. This method was compared with venous angiography and inferior vena cavography prior to, and following, appropriate radiotherapy in a selected group of patients afflicted with neoplastic compression of varying degrees on major venous channels. In addition to angiograms and scintiphotographs, circumference measurements and venous pressures in the affected part were recorded before and after therapy.

With the scintiphotographic technique 10 millicuries of Tc^{99m} pertechnetate were employed intravenously as a bolus in each, the right and left, upper extremity separately, to demonstrate the superior vena cava obstruction. In cases of abdominal or pelvic obstruction, a tributary of the saphenous vein in one, or both, of the lower extremities was injected with a like amount. The scintiphotographs were then made at 2 to 4 second intervals for up to 32 seconds over the general area of obstruction.

Six cases of superior vena cava obstruction and 3 cases of abdominal or pelvic obstruction are reported. The scintiphotographs were found to be initially diagnostic and secondarily useful in the follow-up of the therapeutic result. It was found feasible to do venous pressure recordings and scintiphotographic injections through the same venipuncture. No discouraging effects were encountered from isotopic injections.

Routine fractionation of radiotherapy doses going up to relatively high total doses was carried out in cases of incomplete obstruction to circumvent radiation edema which might lead to complete obstruction. In cases of complete obstruction with well developed collateral circulation a rapid, high dose technique was utilized. No adverse radiation reactions were encountered, and the majority of the patients received excellent palliation.

Sequential scintiphotography was found to be safe and reliable as employed by the authors. The method is advocated as an aid to arriving at the diagnosis, planning radiotherapy and following results. Rapid high dose radiotherapy technique was sucessfully utilized in complete obstruction with good collaterals, and fractionation of dose was used efficaciously where the obstruction was incomplete and the collaterals poorly developed.—*F. C. Petty, M.D.*

Broussin, J., and Martin, P. L. Technique élargie de l'artériographie à contre-courant. (Bordeaux, France.) (Addition to the technique of counter-current arteriography.) *J. de radiol., d'électrol. et de méd. nucléaire*, Aug.-Sept., 1968, *49*, 555–557.

Noting that the development of peripheral vascular studies using complex mechanisms is well known, the authors state that comparable results can be achieved by everyone with simple equipment.

When bilateral femoral injections are made, it is a fact that under relatively moderate pressure the contrast medium mounts higher on the side where there is thrombosis below the needle.

This advantage can be reproduced by the placement of a pneumatic tourniquet inflated to a pressure of 45 to 50 cm. of mercury. Injection then under moderate pressure will permit filling to the aortic bifurcation and to the contra-lateral side. An ad-

ditional injection made just as the tourniquet is released permits visualization of vessels of thigh and leg on the injected side.—*Frank A. Riebel, M.D.*

GENERAL

GONDOS, BELA, Roentgen observations in diabetic osteopathy. *Radiology*, July, 1968, *91*, 6–13. (From: Radiology Division, D. C. General Hospital, 19th and E. Streets, S.E., Washington, D. C. 20003.)

Thirty-eight cases of diabetic osteopathy were reviewed with particular attention to follow-up. The disease involved the toes and/or the metatarsals in 37 of these patients. In half the patients there was involvement of both feet. In 17 patients the disease was of more than 10 years' duration.

The most characteristic feature of diabetic osteopathy is its intermittent course of activity. The process may be inactive for months or years, and the bone in this stage seems to be completely healed. Diabetic osteopathy is generally associated with redness and soft tissue swelling of the part involved or, more commonly, perforating ulcer or gangrene. Some degree of neurologic deficit nearly always accompanies the bone and soft tissue disease. Calcification in the wall of metatarsal and digital arteries is a relatively frequent roentgen observation.

It is important to differentiate between diabetic and arteriosclerotic disease. In diabetic osteopathy and soft tissue necrosis a more conservative surgical approach is usually adequate, while in arteriosclerosis there is frequently a need for major amputation. The patient with diabetic ulcer and osteopathy has little or no pain, the part involved is warm and pink and usually a good pedal pulse is palpable. Changes of arteriosclerotic origin are characterized by manifestations of arterial insufficiency. The part involved is cool, pale, and painful. Bone changes on the roentgenogram are unusual in arteriosclerotic gangrene, even though considerable necrosis may be demonstrated histologically.

Generally the first manifestation of diabetic osteopathy is single fracture or fragmentations, often without a history of trauma. The bone is commonly of normal density but a variable degree of osteolysis may be present. Healing, reconstruction of bone, and reformation of adjacent joints are characteristic features of diabetic osteopathy. The pointed or wedge shape sometimes seen in the metatarsals as the end result of the healing process is also seen in a number of other conditions. It has been noted in progressive systemic sclerosis, following frost bite or burns, rheumatoid arthritis, congenital or surgical amputation, and congenital pseudoarthrosis. The pointed or wedge shape probably represents the result of an exaggerated and modified process of tubulation.

The following 3 factors seem to be responsible for the development of diabetic osteopathy: (a) anesthesia of the part involved; (b) trauma; and (c) a so-far unspecified bone disease (vascular? neurotrophic?).—*A. W. Sommer, M.D.*

RAZZAK, MUHAMMAD ABDEL, HASSABALLA, ABDEL MONEM, and ABOU-KHATWA, HASSAN. Evaluation of the peripheral circulation in diabetics by means of a modified radioisotopic technic. *Radiology*, Sept., 1968, *91*, 568–571. (From: Department of Medicine, University Hospitals, 2065 Adelbert Road, Cleveland, Ohio 44106.)

The common occurrence of peripheral vascular disorders in diabetes mellitus is well documented. An unselected group of diabetics was studied as to the prevalence of such changes in relationship to age, sex, duration of disease and peripheral neuropathy. Calorimetric, oscillometric, and plethysmographic methods were eliminated from this study because of the indirectness of their measure. A common radioisotopic technique was modified to obtain direct quantitative information of blood flow.

Forty-eight diabetic patients, 24 males and 24 females, between 12 and 70 years of age were studied. A complete history was taken, and all patients examined for clinical evidence of peripheral neuropathy and arterial disease.

The procedure room was kept at a constant temperature and draft free. A collimated scintillation detector was placed in contact with the ball of each foot. Thirty microcuries of RISA (I^{131}) was injected intravenously in the antecubital space. The radioactivity was monitored on two strip chart recorders running at 0.75 inch per minute, which were fed by two counting rate meters operating on time constants of 3 seconds. When a plateau was reached the procedure was stopped. Ten mg. of tolazoline hydrochloride (priscol) was given intravenously, and in 3 minutes the procedure was repeated. Isotope doses were standardized by counting the loaded syringes, in air, at a fixed distance prior to injection, and only comparable counting rates were accepted for each patient. Ten drops of KI solution was given by mouth to prevent the thyroidal uptake of radioiodine. The areas under the curves obtained were measured; either by planimetry or calculated: $\text{area} = N_f(t - T\frac{1}{2}/0.693)$; where N_f = radioactivity level at 10 minutes, t = 10 minutes, $T\frac{1}{2}$ = time needed to arrive at 50 per cent of plateau radioactivity.

$$\text{Percentage increase in radioactivity flow} = \frac{\text{measured area before priscol}}{\text{measured area after priscol}} \times 100.$$

Baseline determinations were arrived at on 30 normal volunteers, ages 18 to 34 years. The normal percentage increase of radioactive flow after priscol

was established as 56 ± 17 per cent (mean ± 1 S.D.). The diabetic results were considered abnormal if they were found to be off more than 2 S.D., or less than the lowest limit found in the normal group.

The study was found to be normal in 36 of the 48 diabetics. In 2 patients the right leg was affected, in 2 others the left leg was involved, and in 8 both legs were afflicted. No correlation with sex or duration of disease was established. The older patients, over 50 years, and those with peripheral neuritis exhibited a greater incidence of abnormality. These results are somewhat divergent from those of prior investigators.—*F. C. Petty, M.D.*

RADIATION THERAPY

GOLDBERG, BARRY B., SKLAROFF, DAVID M., and ISARD, HAROLD J. Enchoencephalography in the management of patients receiving radiation therapy. *Radiology*, Aug., 1968, *91*, 363–366. (Address: Dr. D. B. Sklaroff, Department of Radiology, Hahnemann Medical College and Hospitals, Philadelphia, Pa. 19102.)

For over a decade ultrasound has been utilized to locate midline structures of the brain, particularly in evaluating patients with head trauma and suspected brain tumors. The over-all accuracy has reportedly been greater than 94 per cent.

Using echoencephalography, the authors studied 30 patients who received radiation therapy for intracranial tumors, localizing the midline before, during and after therapy. They were able to correlate the degree of displacement with the clinical status of the patient.

The technique and equipment used in this study are detailed. Three individual readings are necessary for each determination, and the study averaged more than 5 determinations per patient.

Fourteen patients had metastatic brain tumors and received 4,000 rads in 4 weeks. Twelve had a good response and echoencephalography disclosed a return of the midline echo to a more medial position.

Sixteen patients with primary brain tumors had midline shifts and 12 of these had a good response to irradiation (average dose 5,500 rads in 5 weeks), while 4 had a poor response. This correlated exactly with the ultrasonographs.

The 6 patients (combined groups) who showed no response to irradiation had a rapid downhill course, both clinically and on their ultrasonographs (increased midline shift).

In 2 patients temporary increase in midline shift was noted after worsening of their symptoms during therapy. When treatment was stopped, both the ultrasonographs and the patients' condition promptly improved. It was concluded that this was due to cerebral edema.

Since there is such a high incidence of brain metastasis in patients who have carcinoma of the lung or breast, echoencephalography can be used routinely in an attempt to detect the lesion early. It can also be used for follow-up after treatment.

When pineal calcification is present, it was found that it shifted in exact correlation with the ultrasonograph.

The advantages of echoencephalography over isotope scanning and arteriography, are that the former is inexpensive, can be done in 5 minutes and the results are promptly available. There is no morbidity.

Echoencephalography is limited to lesions that displace the midline structures. Thus, masses that are small or midline in location are not detectable. This group of patients was less than 40 per cent in the authors' experience, however.—*P. M. Kroening, M.D.*

CHEMOTHERAPY

WOLFF, J. A., KRIVIT, W., NEWTON, W. A., JR., and D'ANGIO, G. J. Single versus multiple dose dactinomycin therapy of Wilms' tumor. *New England J. Med.*, Aug. 8, 1968, *279*, 290–294. (From: The Children's Cancer Study Group A, Babies Hospital, Columbia-Presbyterian Medical Center, 167th Street & Broadway, New York, N. Y. 10032.)

In a controlled co-operative study with 14 groups participating, 64 children were randomized into 2 groups receiving either a single course of dactinomycin (actinomycin D) or maintenance courses given intermittently over a 15 month period.

All patients were 12 months of age or older. All had resectable disease; local extension beyond the kidney did not exclude a patient if an *en bloc* resection was accomplished. Radiation therapy was given according to prevailing usage at each institution in "as standardized a regimen as possible." Dosage, however, ranged from 1,700 to 5,000 rads. All but 5 patients received between 2,000 and 4,000 rads.

A single course of dactinomycin consisted of 5 successive daily doses of 15 μg. per kg. of body weight given intravenously. Patients given maintenance therapy received additional courses 6 weeks and 3 months postoperatively and every 3 months thereafter for 15 months.

Eight patients out of 31 in the single course group and 11 out of 33 in the multiple course group were excluded from follow-up for various reasons. Eleven (48 per cent) of the 23 followed in the single course group were recurrence free at the time of writing, while 19 (86 per cent) of 22 in the multiple course were recurrence free. This difference is statistically significant. It is emphasized, however, that follow-up

is relatively short and further observation is required. —*Howard West, M.D.*

KENNEDY, B. J. Progestogens in the treatment of carcinoma of the endometrium. *Surg., Gynec. & Obst.*, July, 1968, *127*, 103–114. (From: The Department of Medicine, University of Minnesota Medical Center, Minneapolis, Minn.)

The rationale for the use of progestogens in the treatment of endometrial carcinoma is well outlined in the initial portion of this article. From there the author proceeds to an analysis of 75 patients with advanced disease so treated at his institution.

Two progestogens were employed in sequence. The first 41 patients received 17-alpha-hydroxyprogesterone caproate, while the last 34 received dihydroxyprogesterone acetophenide.

Significant, measurable, objective regression (including reduction in size of more than 50 per cent of all tumors and recalcification of osseous lesions with no evidence of progression of any disease) was the only criterion employed for evaluation of tumor response. This occurred in 19 (25.3 per cent) of 75 patients so treated.

In addition, those who did respond showed a satistically significant increase in survival (47 per cent still living) as compared to the non-responders (1.8 per cent still alive). It should be pointed out, however, that the author feels that the patients most likely to be "responders" are those with a long history of disease and slow growing tumors.

The best response was obtained in those patients with pulmonary metastases, while recurrent tumors in intensely irradiated areas are not likely to respond. The mechanism of action of the progestogens in inducing regressions remains to be defined.—*Howard West, M.D.*

THE

THERAPI 4

a clinical linear accelerator of

• LOW COST

Less than the larger Co60 units

Compatible with standard hospital couches

• MINIMUM SPACE



Only 200 sq. ft. room size

Yet full patient set-up flexibility

• HIGH OUT PUTS

4 MeV X-rays

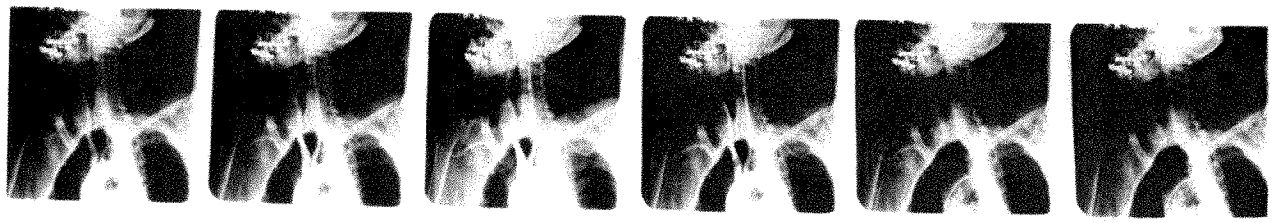
350 R/Min at 80 Cm

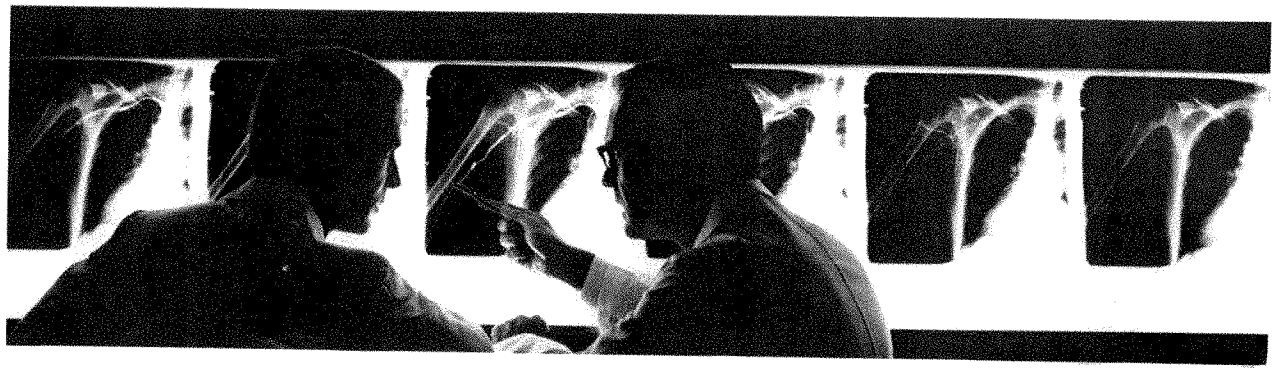
)R FULL DETAILS AND INSTALLATION REQUIREMENTS
WRITE OR CALL:

SHM NUCLEAR
CORPORATIO
568 SAN XAVIE
SUNNYVALE, CALIF. 9408
[408] 245-313

KODAK HAS THE 90-SECOND X-RAY FILM THAT WORKS IN RAPID CHANGERS.

KODAK *RP/S* FILM





Kodak has improved the emulsion design of *RP/S* X-OMAT Medical X-ray Sheet Film to give the transport reliability in rapid changers you've always needed. Yet, you still have 90-second processing

convenience and efficiency.

This is further evidence of the continuing efforts of Kodak to refine and expand the KODAK *RP* X-OMAT® System and all its complements. Everything from the wide choice of x-ray films to improved long-life chemistry and the 90-second KODAK X-OMAT Processor itself.



To try the latest KODAK *RP/S* Film, contact your Kodak Technical Sales Representative. He'll arrange a demonstration of the 90-second film designed to give transport reliability in properly adjusted rapid film changers.

Kodak

EASTMAN KODAK COMPANY
Radiography Markets Division
Rochester, New York

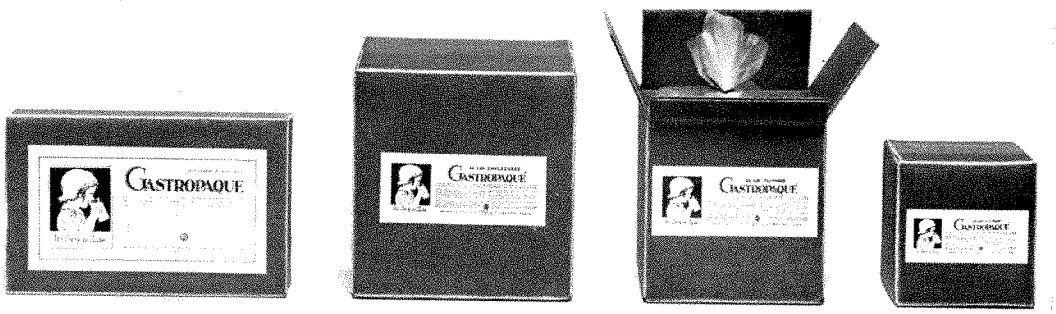
BUCK X-RAY PRODUCTS

1918 — Our 50th Year — 1968

World Famous

GASTROPAQUE®

BARIUM MEAL — *Highest Quality*



20 Dose Package
Flavored only

50 lbs.

25 lbs.

10 lbs

50, 25 and 10 lb. Plastic Lined Cartons Flavored and Unflavored

Unflavored or Vanilla Flavored
Easily Mixed — Stays well in suspension

Does not deteriorate or become rancid with age.

GASTROPAQUE ORDERS SHIPPED SAME DAY RECEIVED

Inquire About Our Attractive Prices
From Your X-Ray Dealer

BUCK X-OGRAPH COMPANY

8709 XOGRAPH AVENUE **ST. LOUIS, MISSOURI 63136**

A recommended course of action for the buyer of radiopharmaceuticals:

1 **INTROSPECTION. Think for a moment. What's your prime concern when you're ready to buy radiopharmaceuticals? Purity? Stability? Availability? Service? Which of these are important to you? Sort them out. Write them down. Give them an order of importance.**

No matter what your analysis reveals, Amersham/Searle Corporation is more than likely to have the solutions. Our range of compounds is wide—from arsenic-74 to xenon-133. Imaging agents for in-vivo investigations. Compounds for in-vitro studies. All with purity and stability of the highest order. All for prompt delivery.

2 **INVESTIGATION. Next, look into the credentials of the suppliers of radiopharmaceuticals. What have they done? What are they doing—in research, in involvement with the field of nuclear medicine itself?**

When you look into Amersham/Searle, the facts are these: A company formed as a joint venture of The Radiochemical Centre, Amersham, England, and G. D. Searle & Co. An organization capable of drawing on the resources of The Centre for radiopharmaceutical research and manufacture. A manufacturer able to utilize the resources of G. D. Searle & Co., a firm long experienced in pharmaceutical research. And a resourceful enterprise capable as well of benefiting from an exchange of information with Nuclear-Chicago Corporation (a Searle subsidiary), designers and manufacturers of nuclear instrumentation.

3 **INFORMATION. Ask to see all available information on the compounds you're interested in. What does the supplier have to say about the radiopharmaceutical? How is it said?**

A Radiopharmaceutical Bulletin from Amersham/Searle is a detailed compilation of facts on every aspect of the compound offered. Clinical information. Biochemical and chemical data. Complete specifications. And extensive bibliographies. Every radiopharmaceutical we make gets the same treatment in our Bulletins.

4 **DECISION: Once you have decided on your probable source of radiopharmaceuticals, make your move. Ask for proof of performance.**

Your phone call or written request to Amersham/Searle will start things moving. We will send complete data on any radiopharmaceutical or attempt to answer any and all questions that go beyond such data. And we'll send you a list of our Telex-connected sales offices. After all, you would expect our actions to speaker louder than our words.

2000 NUCLEAR DRIVE DES PLAINES, ILLINOIS 60018 TELEPHONE: (312) 296-1055



Amersham/Searle

AMERSHAM/SEARLE CORPORATION:
AN ACTIVITY OF G. D. SEARLE & CO. AND THE RADIOCHEMICAL CENTRE

8-216

☐ **THE CARE OF RADIATION CASUALTIES** *by* **John Blakely,** *Medical Officer-in-Charge, United Kingdom Atomic Energy Authority.* '68, 136 pp., 17 il. (1 in color), 10 tables, $5.50

☐ **PLANNING FOR HOSPITAL EXPANSION AND REMODELING** *by* **Donald C. Carner,** *Memorial Hospital of Long Beach, Calif.* '68, 128 pp., 7 il., $8.50

☐ **SURGICAL AND ALLIED MALPRACTICE** *by* **Bernard J. Ficarra,** *Long Island Univ., Greenvale, N.Y. with Forewords by* **Felix Forte** *and* **Anthony J. DiGiovanna.** '68, 1280 pp. (8½ × 11), $60.00

NEW BOOKS FOR ROENTGENOLOGISTS

☐ **INTRODUCTION TO MEDICAL DECISION MAKING** *by* **Lee B. Lusted,** *Loyola Univ. Medical Center, Hines, Ill.* '68, 296 pp. (6¾ × 9¾), 127 il., $18.75

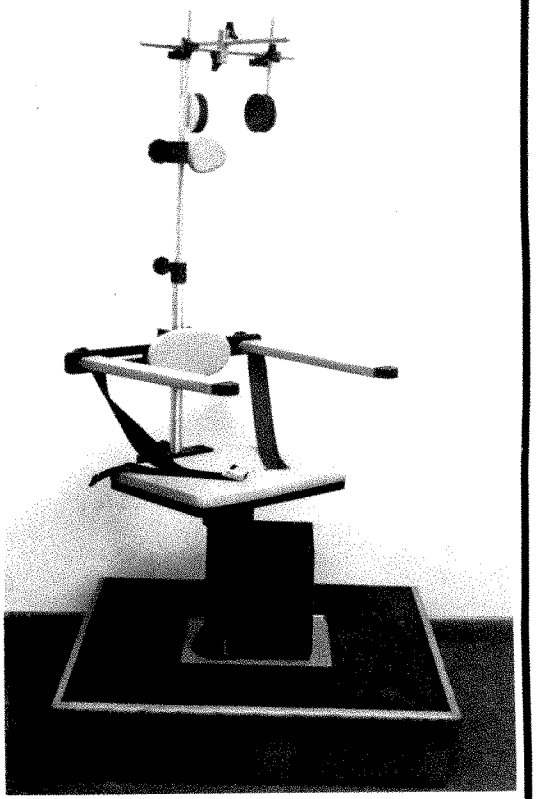
☐ **PEDIATRIC HEAD INJURIES** *by* **John Mealey, Jr.,** *Indiana Univ. School of Medicine, Indianapolis.* '68, 260 pp., 59 il., 15 tables, $10.50

☐ **AIDS TO ETHICS AND PROFESSIONAL CONDUCT FOR STUDENT RADIOLOGIC TECHNOLOGISTS (2nd Ed.)** *by* **James Ohnysty,** *Saint Francis Hosp., Colorado Springs.* '68, 172 pp., $6.75

☐ **ILLUSTRATIVE CRANIAL NEURORADIOLOGY** *by* **Alfred L. Schmitz,** *Univ. of California, Los Angeles;* **Samuel B. Haveson,** *Univ. of Southern California, Los Angeles; and* **Duke Hanna,** *Freeman Memorial Hosp., Inglewood.* '67, 404 pp. (8½ × 11), 532 il. (1 in full color), $31.50

CHARLES C THOMAS PUBLISHER
301-327 East Lawrence Avenue
Springfield • Illinois • 62703

new from BARUCH



baruch therapy chair

First treatment chair expressly designed for the requirements of radiation therapy. Particularly useful for head, neck and upper torso treatments.

The Baruch chair can assist you to

. . . Save time in set-ups.

. . . Position and reposition the patient with minimum disturbance.

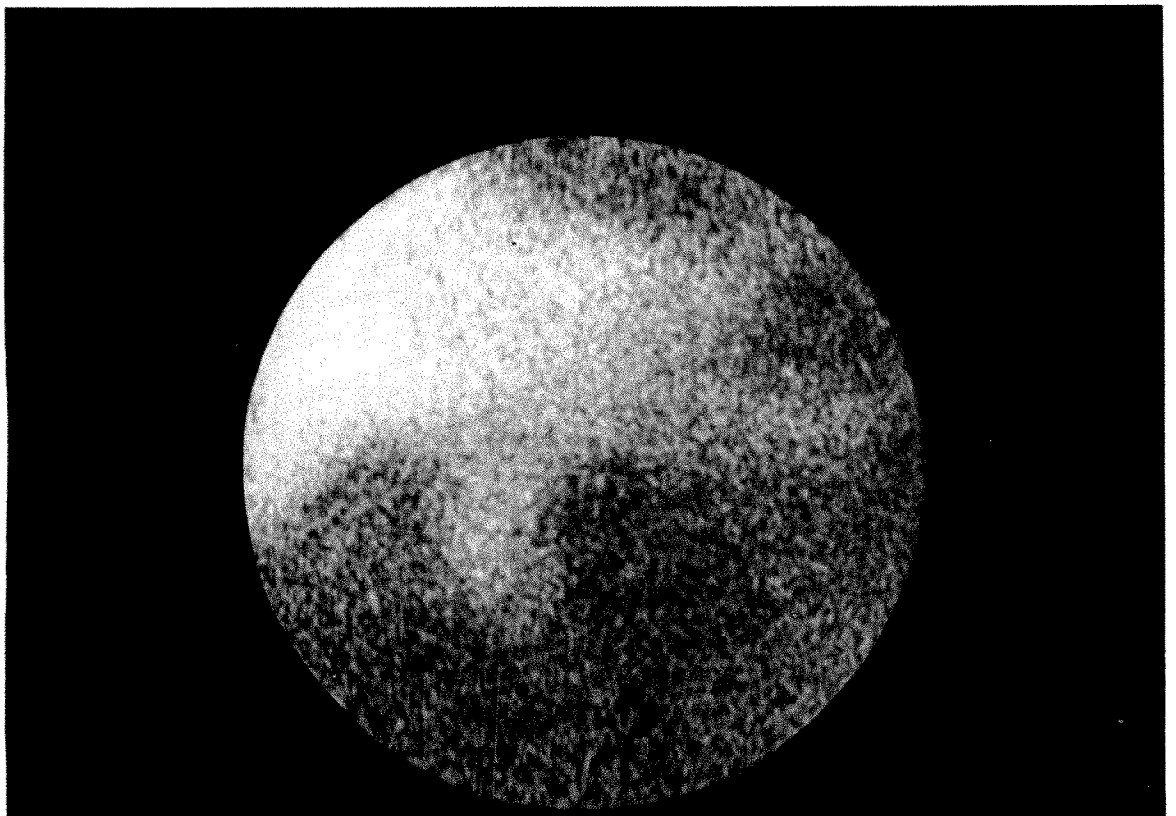
. . . Attain desired accuracy quickly and conveniently.

This mobile chair unit features 21 possible motions—vertical, horizontal, rotational—and a versatile head positioning device. Usable with virtually all existing tele-therapy models.

Ask us for literature describing the Therapy Chair and other accessories for radiation therapy—Baruch specializes in solving your therapy equipment problems.

BARUCH INSTRUMENTS CORPORATION
203 North Highland Avenue
Ossining, New York 10562
(914) 762-2255

Portrait of a Pancreas.



RADIOPHARMACEUTICAL: SELENOMETHIONINE-Se^{75} BY AMERSHAM/SEARLE.

There are many problems inherent in diagnosing diseases of the pancreas by standard radiographic techniques. Further, laboratory determinations are often inconclusive.

Question: Can pancreatic pathology be ruled out as a possible diagnosis short of exploratory surgery?

Answer: Amersham/Searle Corporation now offers the clinician selenomethionine-Se^{75}—a diagnostically reliable imaging agent, especially when used with the gamma scintillation camera for rapid, continuous scintiphotography.

Amersham/Searle's selenomethionine-Se^{75} is of unsurpassed purity and stability. And these qualities are vital to your selection of a drug for your patients. Here are the important specifications for selenomethionine-Se^{75} as supplied by Amersham/Searle:

Stability: Little evidence of radiation decomposition after storage for up to 4 months at room temperature in concentrations of 1 mCi/ml.

Radiochemical purity: >95%.

Chemical purity: >90%.

For further clinical, biochemical, and technical information on L-selenomethionine-Se^{75} (sterile aqueous solution) please write for *Radiopharmaceutical Bulletin RP-1*. Or call us directly.

Indications: Pancreas imaging. **Contraindications:** Radioisotopes should not be administered to patients under 18 years of age, or to pregnant or nursing women, unless invaluable diagnostic information cannot be otherwise obtained. **Precautions:** Observe appropriate radiation-safety procedures at all times. **Availability:** Sterile aqueous solution. Specific activity ranges from 1 to 6 mCi/mg. Radioactivity concentration approximately 250 μCi in 1 ml.

Scintiphoto courtesy D. Bruce Sodee, M.D., Doctors Hospital, Cleveland, Ohio.

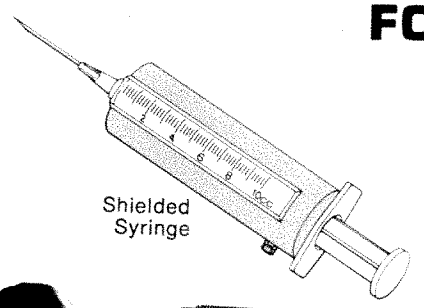
2000 NUCLEAR DRIVE DES PLAINES, ILLINOIS 60018 TELEPHONE: (312) 296-1055

Amersham/Searle

AMERSHAM/SEARLE CORPORATION
AN ACTIVITY OF G. D. SEARLE & CO. AND THE RADIOCHEMICAL CENTRE

8.21a

WHAT'S NEW IN RADIATION SHIELDING FOR NUCLEAR MEDICINE?



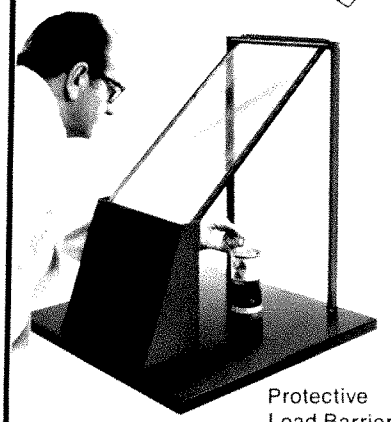
Shielded Syringe

Here is a small sample of the safety shielding now in stock at Nuclear Associates, Inc.... your one source for Nuclear Medicine accessories and supplies.

SHIELDED SYRINGE

Protect your fingers and hands from syringe-administered millicurie quantities of radioactive doses—with the new "Gamma Vue" Syringe Shield.* For example, 8 mc of Tc-99m in an unshielded syringe will expose you to 5,000 mR/hr. The "Gamma Vue" cuts this exposure by a factor of 50; dose rates for I-131 are reduced 4-fold. Consists of 3/16" lead shield with a lead-glass panel for viewing the syringe calibration marks. Tapered lead wall permits minimum interference with venepuncture. Accepts standard disposable syringes.

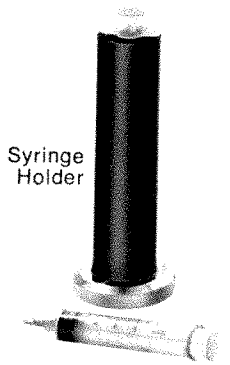
*Patent Pending



Protective Lead Barrier

PROTECTIVE LEAD BARRIER

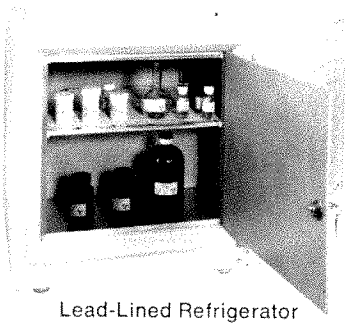
Eliminates radiation to your body or face while milking a Tc-99m generator or other types. Most generators provide enough shielding for the generated activity but not for the setting-up process (e.g., energetic Mo-99 gamma radiation to the face, at 3 feet from a generator, can be as high as 35 mR/hr). All exposure is stopped by a 12" x 12" x 1/2" lead shield and a 12" x 24" lead-glass sheet (4.8 gm/cc).



Syringe Holder

SYRINGE HOLDER

Syringes filled with radioisotopes can be stored or hand-carried safely by inserting them in this special lead cylinder, 3/8" thick x 3/4" I.D. x 5¾" inside depth. Accepts standard 10cc disposable syringes.



Lead-Lined Refrigerator

LEAD-LINED REFRIGERATOR

For radiopharmaceuticals, tagged biological and other radioactive materials requiring low-temperature storage. Key-lock prevents unauthorized access. Completely lead-lined, 1/8" thick. Only 19½" high x 19" wide x 23" deep, small enough to fit on or below a lab bench. Holds 2 cubic ft.

ALSO AVAILABLE

Lead bricks (plain or interlocking), lead-glass bricks, large and small lead storage containers, phantoms, warning signs, remote handling tools, ultrasonic cleaners, dosimeters, monitors, and more.

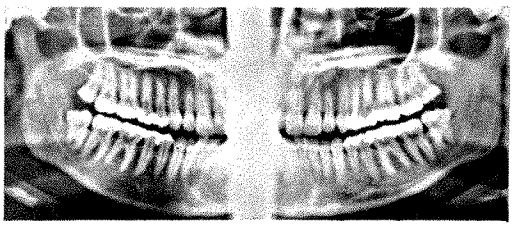
For more details, ask for Catalog NM-68-C

NUCLEAR ASSOCIATES, INC.

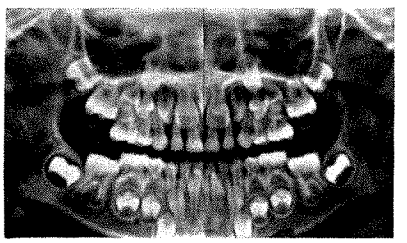
35 URBAN AVENUE, WESTBURY, N.Y. 11590, PHONE (516) 333-9344

A COMPLETE RADIOGRAPH OF THE ENTIRE MOUTH
ON A SINGLE FILM . . . IN SECONDS WITH

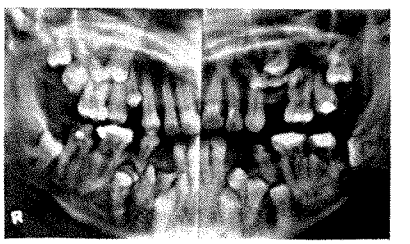
PANOREX®



Panorex gives a clear panorama of all dental structures. Midline and centrals are indicated twice. Clear center area is due to absence of radiation when chair shifts the patient automatically.

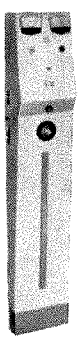


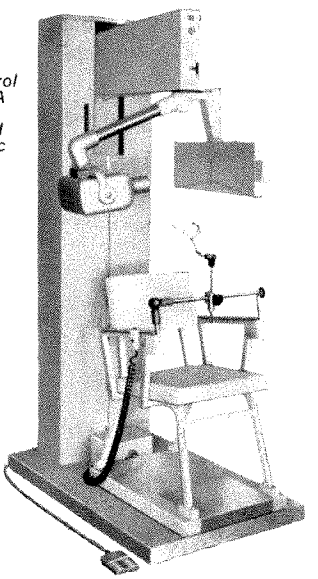
Here the clear center area is eliminated by cutting the film on the midlines. In pedodontics, orthodontics, serial extractions etc., Panorex is unequalled.



Only with Panorex can such diagnostic detail be obtained on an unusual case like this involving many supernumerary teeth. Just one exposure compared to the 14 to 18 for the usual full mouth series.

Remote control 90KV—15MA for both periapical and cephalometric radiography.





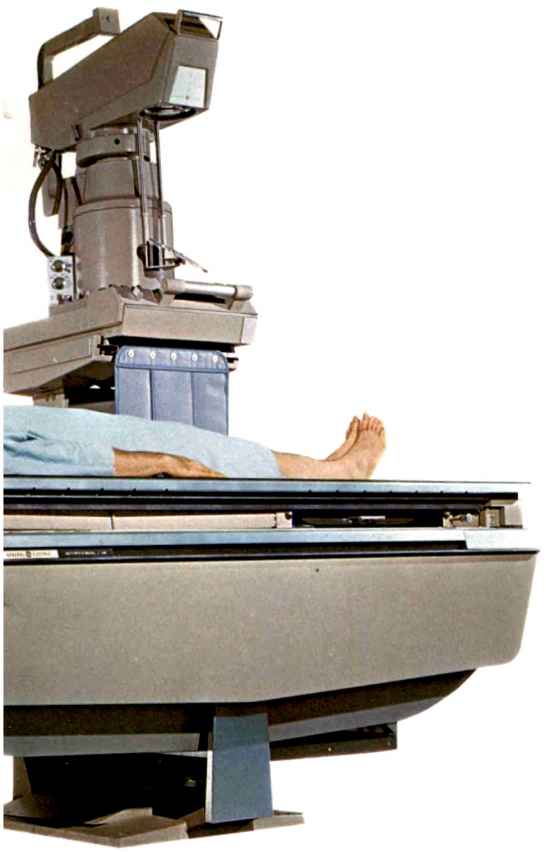
Seating the patient and shooting the picture takes under two minutes with Panorex.® Tubehead rotates around patient's head to record the complete oral cavity. Synchronized film and image conform to dental arch. Chair shifts automatically, changing rotation from one side of the arch to the other while bypassing the spine. X-ray beam is off during shift, and resulting image is essentially uniform in size. Let us tell you more about Panorex, the revolutionary machine that gives a complete radiograph of the entire mouth in 1/10th of the time needed for a full mouth series. Write

S. S. WHITE COMPANY X-RAY DIVISION
A DIVISION OF PENNSALT CHEMICALS CORPORATION
COMMUNITY DRIVE, GREAT NECK, NEW YORK 11021

DIAGNOSTIC X-RAY GENERATORS



From the Power People



Consistency without Compromise. Whatever your procedure, whatever your technic, there is a definite power range you require for the best diagnostic result. That's why General Electric offers the broadest line of diagnostic x-ray generators in the industry. Once you determine your procedural requirements, your GE sales representative will recommend the generator to best suit your needs. In fact, he will work with you, providing knowledgeable suggestions to assure maximum efficiency without compromise.

Variety in generator models is only a part of the GE generator story. Precision design and manufacturing is the real key to consistently excellent results. Our energy conversion experts are sticklers for detail and insist that every component part of every GE generator does its job to perfection. Results are consistent because power output is consistent.

When planning your next x-ray installation, let your GE sales representatives and service technicians take total responsibility for providing you with an equipment-matched power system. The finely tuned system you receive will rarely need service. When it does, the service will be fast and efficient because every GE generator is built with fast access swing-out panels for serviceability.

For consistent results free of procedural compromise and the finest service available call on General Electric —the power people.





Progress is our most important product

GENERAL ELECTRIC

X-RAY DEPARTMENT • MILWAUKEE, WISCONSIN 53201

Improved reliability, even better performance.

Ohio Nuclear's new Model 84FD Dual Five, is the only scanner employing reliable, digital logic, computer-type electronics.

Speeds up to 750 cm./minute produce simultaneous, opposed view photoscans in less than half the time required by other scanners.

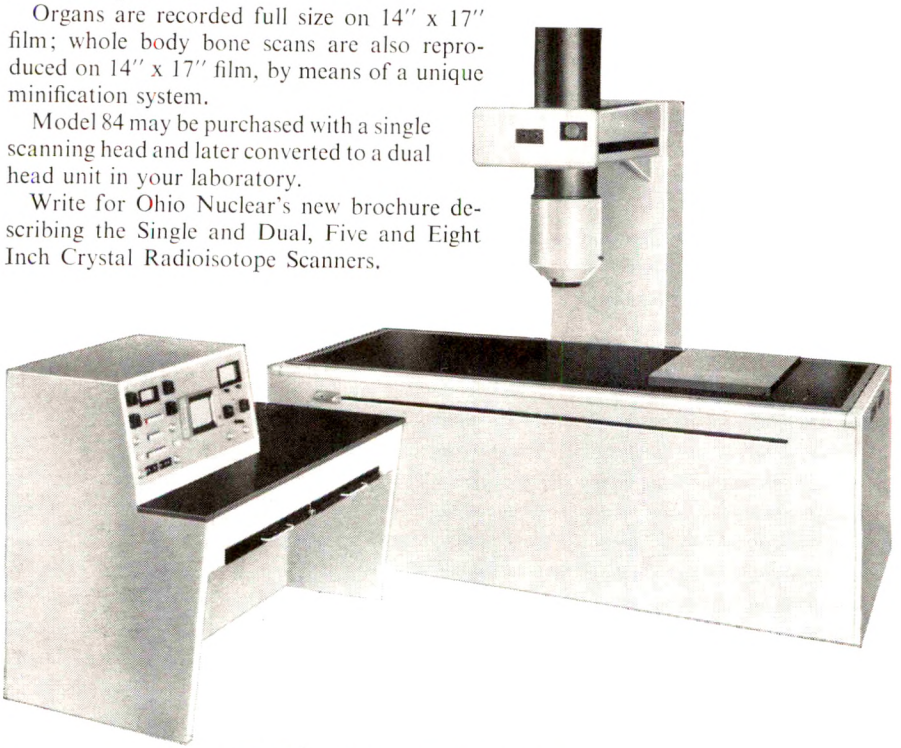
Scan progress is visually monitored on a storage cathode ray tube, which retains the organ image until manually erased.

Simplified pushbutton controls are conveniently located on the desk console. Photo Intensity Computer (PIC) circuit provides consistent, comparable maximum film density at the push of a button. Selectable levels of contrast enhancement and background erase accommodate individual preference.

Organs are recorded full size on 14″ x 17″ film; whole body bone scans are also reproduced on 14″ x 17″ film, by means of a unique minification system.

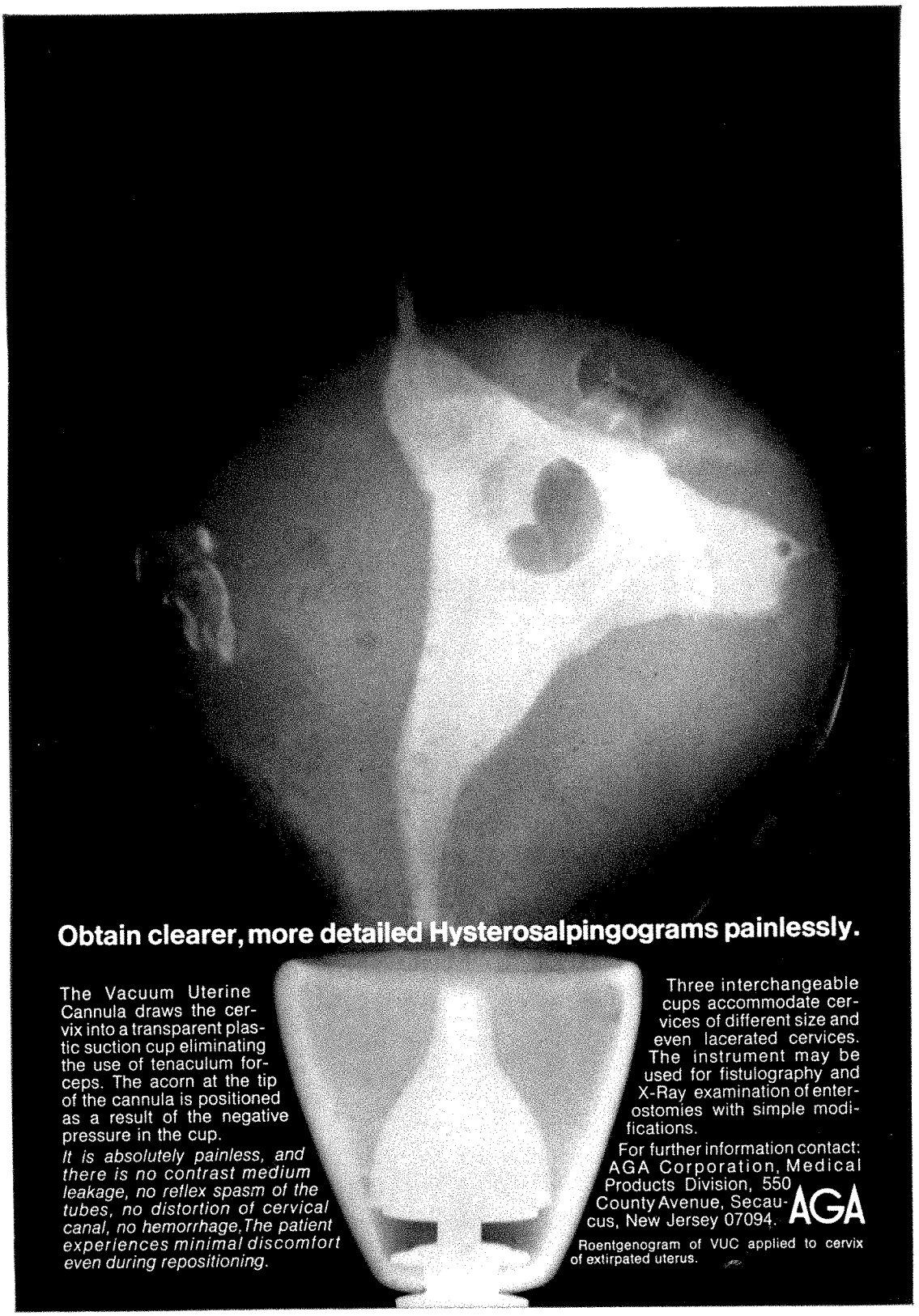
Model 84 may be purchased with a single scanning head and later converted to a dual head unit in your laboratory.

Write for Ohio Nuclear's new brochure describing the Single and Dual, Five and Eight Inch Crystal Radioisotope Scanners.

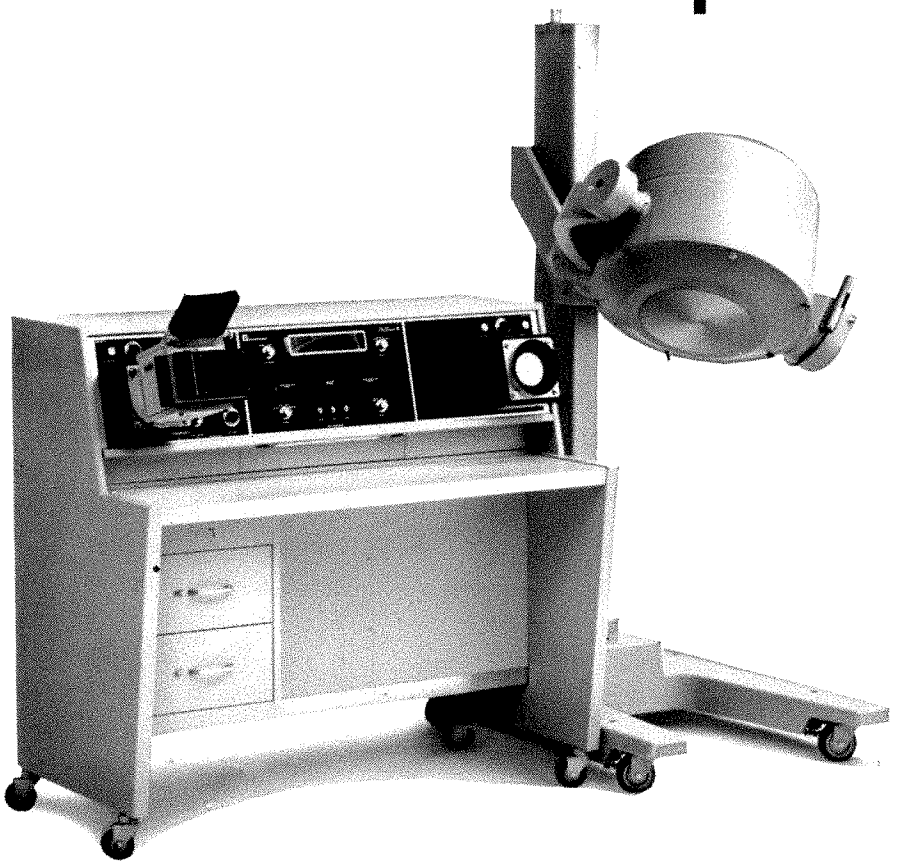


ohio-nuclear, inc.

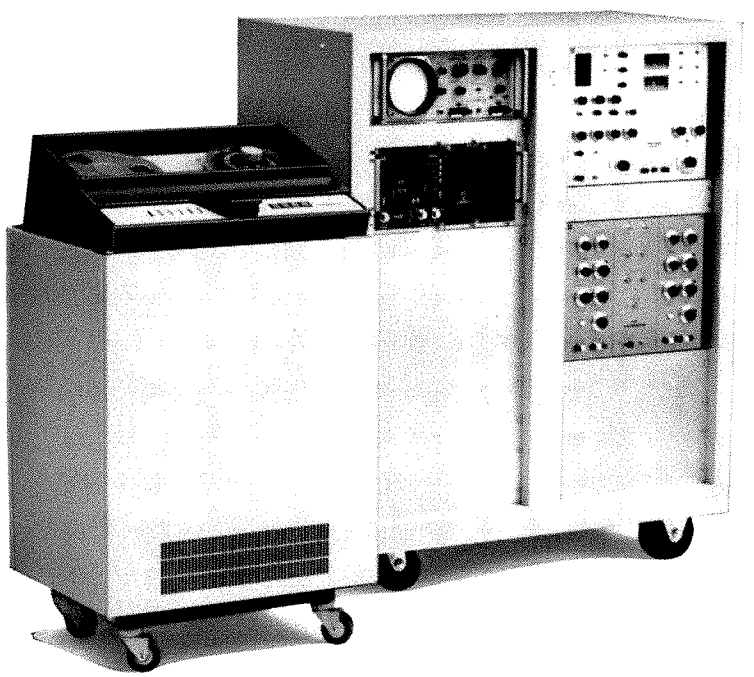
1725 Fall Avenue, Cleveland, Ohio 44113 (216) 621-8142


Obtain clearer, more detailed Hysterosalpingograms painlessly.
The Vacuum Uterine Cannula draws the cervix into a transparent plastic suction cup eliminating the use of tenaculum forceps. The acorn at the tip of the cannula is positioned as a result of the negative pressure in the cup.
It is absolutely painless, and there is no contrast medium leakage, no reflex spasm of the tubes, no distortion of cervical canal, no hemorrhage.The patient experiences minimal discomfort even during repositioning.
Three interchangeable cups accommodate cervices of different size and even lacerated cervices. The instrument may be used for fistulography and X-Ray examination of enterostomies with simple modifications.
For further information contact: AGA Corporation, Medical Products Division, 550 County Avenue, Secaucus, New Jersey 07094.
AGA
Roentgenogram of VUC applied to cervix of extirpated uterus.

Now – the Pho/Gamma® III Scintillation Camera talks to computers.



And listens.



How? With our new computer-compatible Magnetic Tape System.

The two instrument consoles shown directly above constitute our Magnetic Tape System. In the console on the right is our multidimensional analyzer. It connects to the Pho/Gamma III Scintillation Camera. This combination provides analog-to-digital conversion of data on the location and distribution of gamma-emitting radioisotopes in body organs.

The analyzer also encodes the data, in computer-compatible form. And then transfers the data to the second console (above left), the magnetic tape transport.

So much for theory. Application is where the Magnetic Tape System pays off. Because the taped data on a multitude of clinical organ studies can now be fed to a programmed off-line computer.

Which then does what a computer is meant to do—analyze, correlate, and manipulate data. To let you find out more, in more ways. New ways.

Of course you can play back the tape. And re-display and re-orient the data on the analyzer's scope. Then photograph the scope display. Or read out the data on a digital printer. Or—well, you're sure to find more to do with data in a convenient, permanent taped form.

But first you should talk to your Nuclear-Chicago sales engineer about the Magnetic Tape System for Pho/Gamma III. And about our other new Pho/Gamma III accessories (fast digital printer, chart recorder, and 35-mm automatic time-lapse camera, among others). Or, if you'd like, write directly to us. 8-039

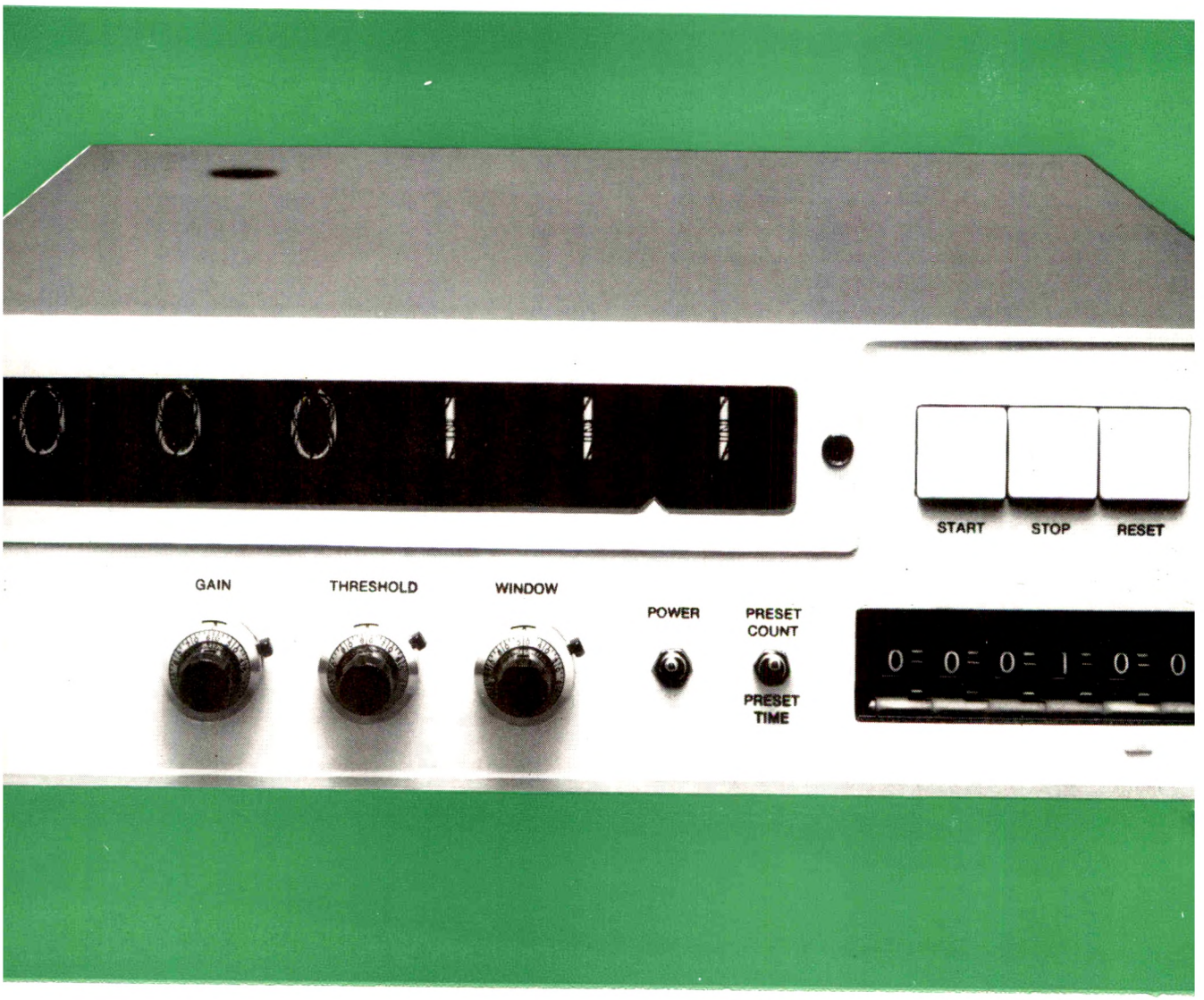
Research in the Service of Mankind

NUCLEAR-CHICAGO CORPORATION

A SUBSIDIARY OF G. D. SEARLE & CO.

307 East Howard Avenue
Des Plaines, Illinois 60018, U.S.A.
Donker Curtiusstraat 7, Amsterdam W.

Abbott Laboratories is now



This is the
LOGIC™ Well Counter–
only inches larger than this page
(12¼″ x 4 1/16″ x 13″ to be exact)

TM—TRADEMARK

in Nuclear Instruments



The LOGIC Series—the most compact counting systems ever designed—is available now in 3 models.

The LOGIC Counting Systems offer:

804468

- Compactness (micrologic integrated circuitry)
- Dependability (pre-tested for 40 hours)
- Portability (25-35 lbs.)
- Versatility (choice of 3 models)
- Quality (backed by Abbott)

For more information, contact your Abbott man who knows both instruments and radio-pharmaceuticals

ABBOTT LABORATORIES NORTH CHICAGO, ILLINOIS
Abbott Laboratories, S.A., 2, rue Thalberg, 1201 Geneva, Switzerland

INDEX TO ADVERTISERS

Abbott Laboratories ..... xxiv, xxv, lviii, lix
AGA Corporation lv
Amersham/Searle Corporation ..... xlvii, xlix
Atomic Energy of Canada Ltd. xiii

Barnes-Hind Barium Products ..... xiv, xv
Baruch Instruments Corporation xlviii
Buck X-Ograph Company xlvi

duPont, E. I., de Nemours Co. ..... xvi, xvii

Eastman Kodak Company ..... xliv, xlv
Elema-Schonander, Inc. xviii

Flow Pharmaceuticals, Inc. xxxi

GAF Corporation ..... xxviii, xxix
General Electric Company ..... lii, liii

Halsey X-Ray Products Company xix
High Voltage Engineering i

Ilford, Inc. vi

Keleket X-Ray Corporation xx

Machlett Laboratories, Inc. ..... xxi, xxii
Mallinckrodt/Nuclear Radiopharmaceuticals xxvi
Mosby, C. V. Company, The xxxv

Nedmac, Inc. xxx
North American Philips Company ..... ix, x, xi, xii
Nuclear Associates, Inc. l
Nuclear-Chicago Corporation ..... lvi, lvii

Ohio-Nuclear, Inc. liv
Ortho Pharmaceutical Corporation xxxiv

Pako Corporation xlii
Pharos Viewing Equipment Co. lxii
Picker Nuclear Corporation ..... Second Cover
Picker X-Ray Corporation ..... xxxix, Fourth Cover
Profexray, Inc. ..... xxxii, xxxiii
Purdue Frederick Company, The v

Schick X-Ray Company xxiii
SHM Nuclear Corporation xliii
Siemens Medical of America, Inc. xxvii
Standard X-Ray Company viii

Thomas, Charles C, Publisher ..... xlviii, lxi

Varian Radiation Division ..... xl, xli

S. S. White Company li
Winthrop Laboratories ..... vii, xxxvi, xxxvii, xxxviii
Wolf X-Ray Corporation ..... Third Cover

•

We try to present an accurate index. Occasionally this may not be possible because of a last-minute change or an omission.

RECOMMENDED READING FOR ROENTGENOLOGISTS

- **SELECTIVE RENAL ARTERIOGRAPHY: Its Application to the Diagnosis of Renal Vascular and Parenchymal Lesions** *by* **Ivan L. Bunnell,** *State Univ. of New York at Buffalo.* '68, 248 pp. (6¾ × 9¾), 183 il., $18.75

- **X-RAY DIAGNOSIS OF CONGENITAL CARDIAC DISEASE** *by* **Larry P. Elliott** *and* **Gerold L. Schiebler,** *both of Univ. of Florida College of Medicine, Gainesville. Foreword by* **Paul C. Hodges.** '68, 260 pp., 221 il., 3 tables, $11.50

- **ROENTGENOGRAPHIC DIAGNOSIS OF BLADDER TUMORS** *by* **Erich K. Lang,** *Methodist Hosp., Indianapolis.* '68, 132 pp. (7 × 10), 94 il., 11 tables, $9.75

- **HODGKIN'S DISEASE** *compiled and edited by* **David W. Molander,** *Cornell Univ. Medical College, and* **George T. Pack,** *New York Medical College. Both of New York City. (7 Contributors)* '68, 228 pp. (7 × 10), 121 il., 39 tables, $15.00

- **SOLITARY METASTASES** *by* **Philip Rubin,** *Univ. of Rochester Medical Center, New York, and* **Jerold Green,** *Zellerbach Saroni Tumor Institute, Mount Zion Hosp., San Francisco.* '68, 268 pp., 153 il., 30 tables, $14.75

- **LUNG CALCIFICATIONS IN X-ray Diagnosis** *by* **Emanuel Salzman,** *Univ. of Colorado School of Medicine, Denver.* '68, 132 pp. (6¾ × 9¾), 74 il., $7.50

- **CERVICAL SPONDYLOSIS AND ITS NEUROLOGICAL COMPLICATIONS** *by* **Bernard H. Smith,** *State Univ. of New York at Buffalo.* '68, 240 pp. (6¾ × 9¾), 101 il., $12.00

FUNDAMENTAL PROBLEMS IN SCANNING *compiled and edited by* **Alexander Gottschalk** *and* **Robert N. Beck,** *both of Univ. of Chicago. (38 Contributors)* Actual and hypothetical systems are described to illustrate discussions of the fundamental issues. New concepts involving analog and digital computer techniques, tomographic scanning, information theory, and visual perception are employed in discussing approaches to these problems. *'68, 424 pp. (7 × 10), 309 il. (10 in full color), 12 tables, $26.75*

CANCER THERAPY BY INTEGRATED RADIATION AND OPERATION *compiled and edited by* **Benjamin F. Rush, Jr.,** *and* **Robert H. Greenlaw,** *both of Univ. of Kentucky College of Medicine, Lexington. Foreword by* **Charles Tucker.** *(40 Contributors)* Covers basic experimental data concerning combined therapy, dosage, time of treatment, types of treatment, and interrelation of treatment. Definitive conclusions reached are indicated—current trends explained. *'68, 176 pp. (7 × 10), 58 il., 82 tables, $12.75*

NORMAL RADIOLOGICAL ANATOMY: Radiological Optics and Film Interpretation *by* **Henry Tillier,** *Late Professor of Radiology, Algiers. Translated and edited by* **Ronan O'Rahilly,** *St. Louis Univ. School of Medicine.* The laws of radiological optics are presented with application to the skeletal system. Commonly used projections are described and illustrated, with complicated areas built up in stages. *'68, 400 pp., 375 figs., 3 tables, $12.50*

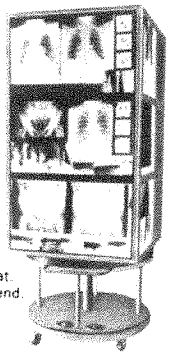
ADVANCES IN DYNAMIC RADIOACTIVE SCANNING *compiled and edited by* **Yen Wang,** *Univ. of Pittsburgh. (10 Contributors)* For the use of radioactive nuclides in clinical diagnosis and research . . . *newly developed techniques and applications in dynamic scanning with radioactive nuclides are described.* Applications of thyroid scanning using gamma camera, parathyroid scanning, and pancreatic scanning are included. *'68, 140 pp., 101 il., 7 tables, $8.50*

A complete list of books in this field sent free on request

CHARLES C THOMAS • PUBLISHER 301-327 East Lawrence Avenue **SPRINGFIELD • ILLINOIS 62703**

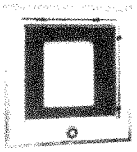
"ROTATABLE"
ILLUMINATOR

• High performance film viewing device • Continuous un-interrupted film inspection • Simultaneous loading, viewing and unloading • Practically unlimited capacity



Pat. Pend.

MOTOR DRIVEN OR MANUALLY OPERATED • UN-INTERRUPTED ROUND-THE-CLOCK VIEWING



"CURTAINED" ILLUMINATOR: 17x17 in. to spot size viewing area with stepless light intensity control essential for high quality film inspection and providing unequalled detail perceptibility.

"MASKING ATTACHMENT": New shutter arrangement applicable to the conventional curtainless 14x17 in. illuminator making it a high performance viewing instrument with full diaphragming facilities.



PHAROS VIEWING EQUIPMENT

FOR ADDITIONAL INFORMATION: Contact your X-ray Supply Company or PHAROS VIEWING EQUIPMENT.
132 MYRTLE AVE., FORT LEE, N.J. 07024



YOU CAN ACQUIRE VALUABLE BACK VOLUMES AND SINGLE ISSUES OF THE PUBLICATIONS OF

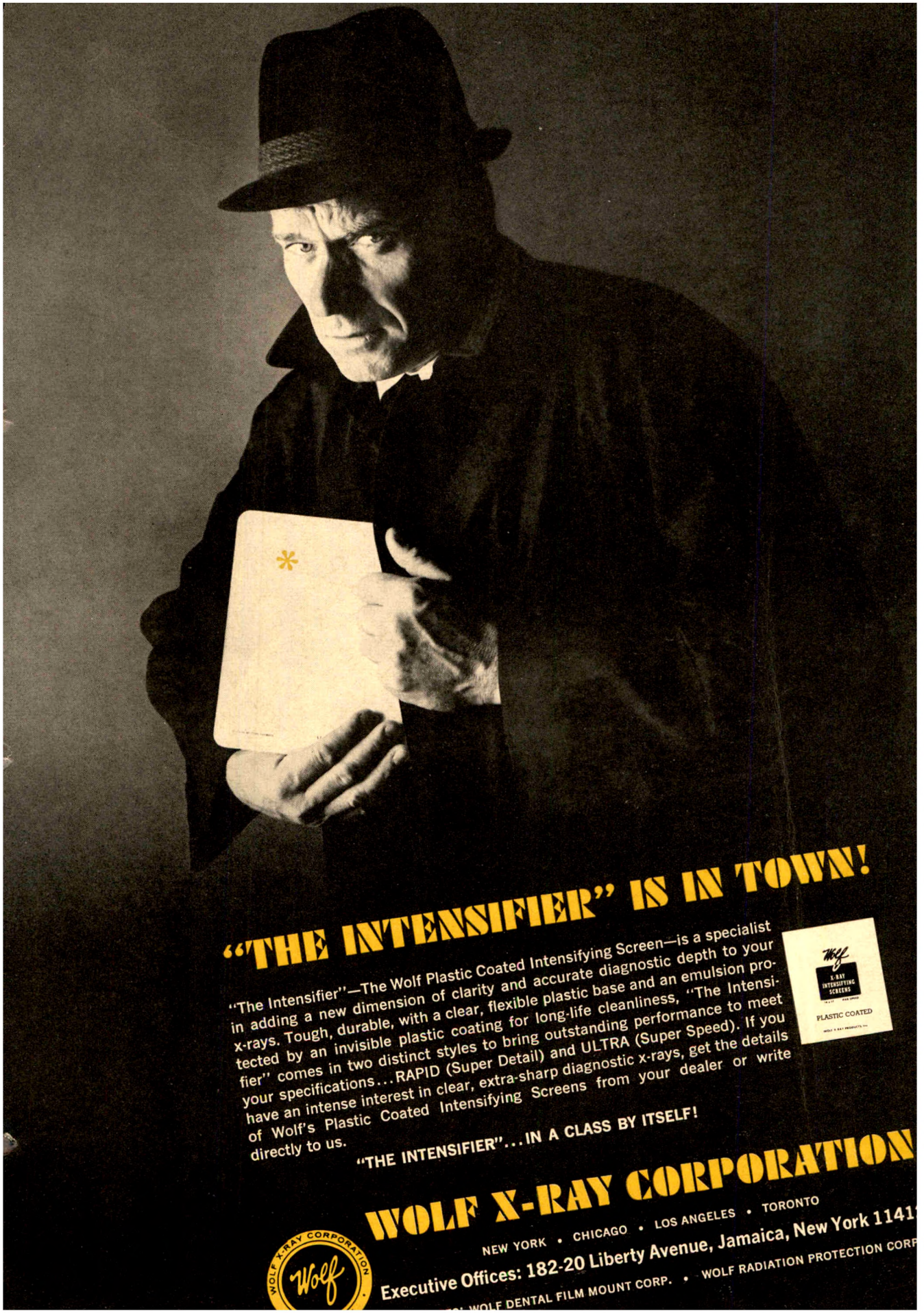
The American Roentgen Ray Society

A limited quantity of the issues available are listed below. Orders are subject to the exhaustion of available stock. This offer is subject to withdrawal without notice. **NOTE: For your convenience, the same price—$2.00 per copy—applies to all issues—no quantity discount.**

Order BACK ISSUES of the Journal from:
CHARLES C THOMAS • PUBLISHER 301-327 East Lawrence Ave. SPRINGFIELD • ILLINOIS

The American Journal of Roentgenology, Radium Therapy and Nuclear Medicine: 1951-1967

Vol. 65, Nos. 1, 2, 4, 5, 6 (1951)
Vol. 66, Nos. 1-6 (July-Dec. 1951)
Vol. 67, Nos. 1, 3, 4, 5, 6 (1952)
Vol. 68, Nos. 1-6 Inclusive (July-Dec. 1952)
Vol. 69, Nos. 1, 2, 3, 4, 6 (1953)
Vol. 70, Nos. 1-6 Inclusive (July-Dec. 1953)
Vol. 71, Nos. 1-6 Inclusive (Jan.-June 1954)
Vol. 72, Nos. 1-6 Inclusive (July-Dec. 1954)
Vol. 73, Nos. 1-6 Inclusive (Jan.-June 1955)
Vol. 74, Nos. 1-6 Inclusive (July-Dec. 1955)
Vol. 75, Nos. 1-6 Inclusive (Jan.-June 1956)
Vol. 76, Nos. 1-3-4-5-6 (1956)
Vol. 77, Nos. 1-6 Inclusive (Jan.-June 1957)
Vol. 78, Nos. 1-6 Inclusive (July-Dec. 1957)
Vol. 79, Nos. 3, 5 (Mar., May 1958)
Vol. 80, No. 6 (June 1958)
Vol. 81, No. 5 (May, 1959)
Vol. 83, Nos. 1-6 Inclusive (Jan.-June 1960)
Vol. 84, Nos. 1-6 Inclusive (July-Dec. 1960)
Vol. 85, Nos. 1-6 Inclusive (Jan.-June 1961)
Vol. 86, Nos. 1-6 Inclusive (July-Dec. 1961)
Vol. 87, Nos. 1-6 Inclusive (Jan.-June 1962)
Vol. 88, Nos. 1-6 Inclusive (July-Dec. 1962)
Vol. 89, Nos. 1-6 Inclusive (Jan.-June 1963)
Vol. 90, Nos. 1-6 Inclusive (July-Dec. 1963)
Vol. 91, Nos. 1-6 Inclusive (Jan.-June, 1964)
Vol. 92, Nos. 1-6 Inclusive (July-Dec. 1964)
Vol. 93, Nos. 1-4 Inclusive (Jan.-April, 1965)
Vol. 94, Nos. 1-4 Inclusive (May-Aug. 1965)
Vol. 95, No. 1 (Sept. 1965)
Vol. 97, Nos. 1, 2, 4 (May, June, Aug. 1966)
Vol. 98, Nos. 1-4 Inclusive (Sept.-Dec. 1966)
Vol. 99, Nos. 1-4 Inclusive (Jan.-April, 1967)
Vol. 100, Nos. 1-4 Inclusive (May-Aug. 1967)
Vol. 101, Nos. 1-4 Inclusive (Sept.-Dec. 1967)
Vol. 102, Nos. 1-4 Inclusive (Jan.-April, 1968)
Vol. 103, Nos. 1-4 Inclusive (May-Aug. 1968)
Vol. 104, Nos. 1-3 Inclusive (Sept.-Oct.-Nov. 1968)



"THE INTENSIFIER" IS IN TOWN!

"The Intensifier"—The Wolf Plastic Coated Intensifying Screen—is a specialist in adding a new dimension of clarity and accurate diagnostic depth to your x-rays. Tough, durable, with a clear, flexible plastic base and an emulsion protected by an invisible plastic coating for long-life cleanliness, "The Intensifier" comes in two distinct styles to bring outstanding performance to meet your specifications... RAPID (Super Detail) and ULTRA (Super Speed). If you have an intense interest in clear, extra-sharp diagnostic x-rays, get the details of Wolf's Plastic Coated Intensifying Screens from your dealer or write directly to us.

"THE INTENSIFIER"... IN A CLASS BY ITSELF!

WOLF X-RAY CORPORATION

NEW YORK • CHICAGO • LOS ANGELES • TORONTO

Executive Offices: 182-20 Liberty Avenue, Jamaica, New York 1141

WOLF DENTAL FILM MOUNT CORP. • WOLF RADIATION PROTECTION CORP

Somewhere near you, a radiologist is getting the sharpest images he's ever seen because of this new table.

3C MAY 1969

Hundreds of radiologists now working with the new Picker "Galaxy" table are getting the best images they've ever experienced: the sharpest fluoroscopy, spotfilms, and Bucky radiographs. And because their everyday practical experience is likely to be more revealing than our technical explanations, you might wish to seek out a current user of the "Galaxy" table. (If you need help with this search, let us know. We'll help you set up a visit.)

Until then, the following technical explanations can provide background as to why the "Galaxy" table produces such superb images.

The table is so structurally rigid that it thoroughly tames the subtle (and some not-so-subtle) vibrations all too often encountered in x-ray tables. The improvement in image sharpness resulting from such suppression is dramatic.

The "Galaxy" collimating system optimizes imaging geometry by significantly refining the relationship of focal spot, shutter plane, film plane, and patient plane. Geometric unsharpness and penumbra, for instance, are abated by locating the fluoroscopic shutter 30% farther from the focal spot than is customary.

Another important point about the "Galaxy" system is the way its automatic coning improves radiographic contrast, reduces scatter radiation, and minimizes dosage to patients and operators.

And now for help in finding a nearby "Galaxy" table user to speak to—or for more information from us—contact your local Picker representative or write Picker Corporation, 595 Miner Road, Cleveland, Ohio 44143.

PICKER

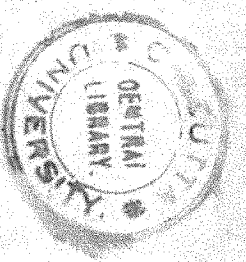


FOUNDED IN 1906 AS THE AMERICAN QUARTERLY OF ROENTGENOLOGY

THE AMERICAN JOURNAL OF ROENTGENOLOGY RADIUM THERAPY AND NUCLEAR MEDICINE

OFFICIAL ORGAN OF

THE AMERICAN ROENTGEN RAY SOCIETY
THE AMERICAN RADIUM SOCIETY



TRAIAN LEUCUTIA, Editor
KENNETH L. KRABBENHOFT, Assistant to the Editor

ASSOCIATE EDITORS

HARRY HAUSER RUSSELL H. MORGAN EDWARD B. D. NEUHAUSER

CONSULTING EDITORIAL BOARD

OSCAR V. BATSON
JOHN CAFFEY
ROSS GOLDEN
PAUL C. HODGES
HOWARD B. HUNT
JOHN H. LAWRENCE
REED M. NESBIT
EUGENE P. PENDERGRASS
LAURISTON S. TAYLOR
OWEN H. WANGENSTEEN
SHIELDS WARREN

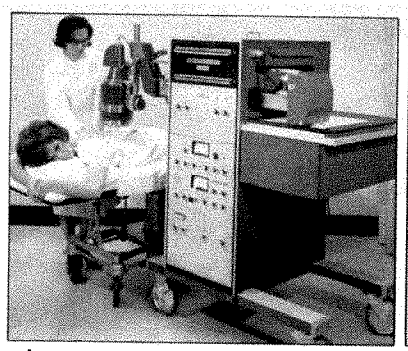
Issued Monthly for the American Roentgen Ray Society by

CHARLES C THOMAS · PUBLISHER · SPRINGFIELD · ILLINOIS · 62703

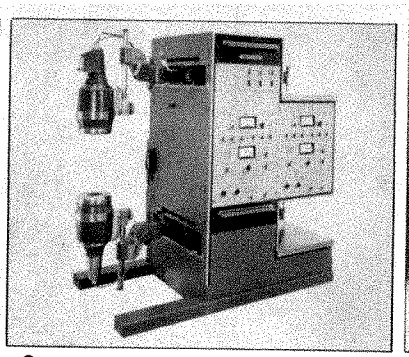
VOLUME 105 FEBRUARY, 1969 NUMBER 2

Fifty-first Annual Meeting, American Radium Society
Bellevue Stratford Hotel, Philadelphia, Pennsylvania 19102
April 27-30, 1969

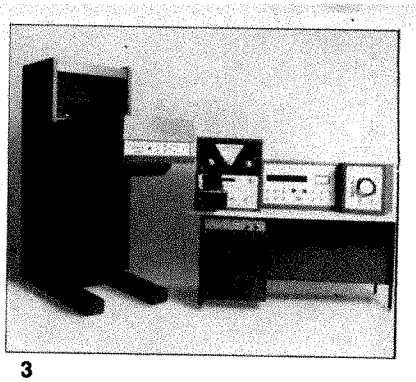
For Preliminary Program see January Issue



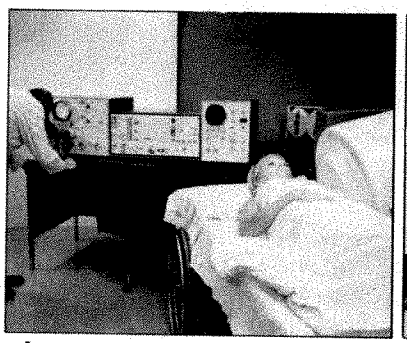
1



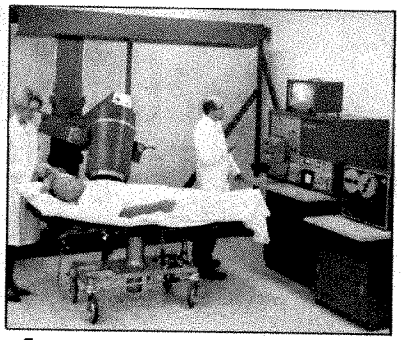
2



3



4



5

1 Magnascanner® 500

2 Dual Magnascanner®

3 Dynapix®

4 Dynacamera™

5 Magnacamera®

"Which is the better choice for gamma imaging, a scanner or a camera?"

(Yes.)

That's much like: "which is better: a plane or a car?" Surely it depends upon the problem at hand.

As it does with gamma imaging. Your one best bet might well be a scanner. Or a camera. You may need both. Sadly, there can be no universal instrument, no all-things-to-all-men system. Consequently, Picker now offers five separate and distinct imaging devices: three are scanners, two are cameras. And this is the most complete line in the world. By far.

The implication is simple: the chances are excellent that Picker has the specific system that precisely matches your needs. Here now are some recognizable user requirements coupled with the appropriate Picker instruments.

Need: small hospital, starting static-imaging, small patient load, modest budget. Or: large hospital needing additional diagnostic confirmation. Solution: Magnascanner® 500. Four out of five nuclear medicine departments start with a Magnascanner. Now over 2000 in use throughout the world. Despite many new features and very high resolution, cost is modest.

Need: specialized static studies involving two views at same time. Solution: Dual Magnascanner®. Provides two large, high resolution scans simultaneously.

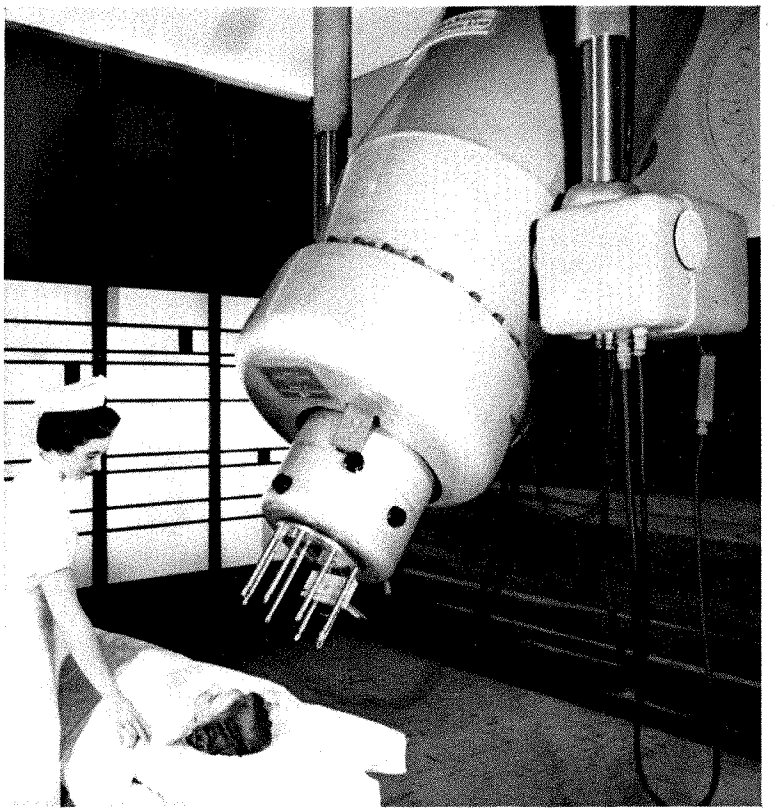
Need: heavy static-imaging patient load. Some demand for dynamic function work also. Solution: Dynapix®. High speed static imaging with very high resolution. Also useful for medium speed dynamic function studies.

Need: broad capability for handling both static imaging and dynamic function (and a great deal of it). Solution: Dynacamera™. Very fast instrument providing high resolution. Does both static and dynamic work.

Need: sophisticated dynamic function work at very high speeds. Solution: Magnacamera®. Exceptionally high speed for studying the most rapid dynamic processes.

The conclusion: Picker has a wide selection of imaging systems because there are many imaging needs. The *widest* selection in the world. Suggestion: describe your situation to your local Picker representative and ask him to develop solutions. Or, if more convenient, start by requesting our detailed gamma-imaging brochure. Write Picker Nuclear, 1275 Mamaroneck Avenue, White Plains, N.Y. 10605. Dept. P

PICKER

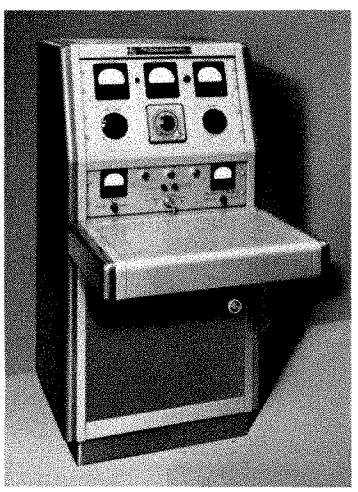


Improved Model AM Van de Graaff is the result of experience gained in 40 previous installations.

IMPROVED *Van de Graaff*® ACCELERATOR MEETS THE MODERN NEED FOR LOW-COST PRECISION THERAPY

Today's Model AM 2 MeV Van de Graaff Therapy Unit continues to keep pace with the trend to low-cost precision therapy in leading hospitals and cancer clinics throughout the Free World. And for five good reasons:

- Its less than 3 mm "point source" of x-rays allows optimum technics for both large and small treatment fields.
- Its treatment beam is accompanied by negligible penumbra.
- Its Roentgen output exceeds that of a 5000 curie cobalt source.
- Its x-ray output will not fall off. You can hold treatment techniques and parameters constant.
- It can be operated easily by a technician without a staff physicist in attendance.



The Model AM Van de Graaff is a reliable, proven source of high-energy radiation. It offers more roentgens-per-dollar and has demonstrated less overall cost-per-treatment than any other comparable supervoltage source available today — including radioisotopes.

Full time use of the reliable Model AM 2 MeV Van de Graaff Therapy Unit will amplify your technic range and expand your patient handling capacity. It is backed by the international reputation of the leading manufacturer of particle accelerators — High Voltage Engineering Corporation. Write Medical Sales.

Today's Model AM is routinely operated by an easily-trained technician.

HIGH VOLTAGE ENGINEERING CORPORATION
BURLINGTON, MASSACHUSETTS

GENERAL INFORMATION

Manuscripts offered for publication and other correspondence relating to the editorial management and books for review should be sent to Dr. Traian Leucutia, Editor, 401 Professional Building, Detroit, Michigan 48201. Contributions may be sent in foreign languages and will be translated if found acceptable. Original articles are published with the understanding that they are contributed exclusively to THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE.

A certain number of illustrations will be supplied free of cost; but special arrangements must be made with the Editor and Publisher for excess illustrations and elaborate tables.

Fifty reprints are furnished without charge to authors. Additional reprints may be purchased according to a scale of prices that accompanies galley proofs. As soon as each issue is printed, the type is destroyed except for reprint orders *in hand*. Reprint orders *must* be returned with corrected galley proof to the Editorial Office if additional reprints are desired.

Correspondence regarding subscriptions, advertisements, and other business relating to THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE should be addressed to Charles C Thomas, Publisher 301–327 East Lawrence Avenue, Springfield, Illinois 62703. (All requests to be submitted in writing.)

Manuscripts should be typewritten, with double spacing, and good margins (not on thin paper) and the *original* should be sent to the Editor. The author should keep a carbon copy, as the original is not returned. The name of the author should appear on each sheet of manuscript. Tabular materials should be typed on separate sheets; likewise bibliographical lists, footnotes, etc.

Drawings and charts for reproduction should be made in black (*never* in blue). Photographic prints of plates or slides on glossy paper produce the best half-tones.

All photographs and drawings intended for illustrations should be numbered, the top plainly indicated, and an abbreviated title of the paper placed on the back of *each one*.

Legends for illustrations should be typewritten in a single list, double spaced, with numbers corresponding to those on the photographs and drawings, instead of attaching each legend to its corresponding figure.

Care in preparation of bibliographies will save much time and correspondence. Each reference in a bibliography should include the following information in the order indicated: Name of the author with initials; title of the article; name of the periodical; year, volume and pages. It is requested that the authors use the following as model:

1. Olcott, C. T., and Dooley, S. W. Agenesis of lung of infant. *Am. J. Dis. Child.*, 1943, *65*, 766–780.

The month should be given if the reference is to an issue of the current year. An alphabetical arrangement of the authors is requested.

The author should always place his full address somewhere on his manuscript. This is very important and is often omitted.

For information regarding membership in the American Roentgen Ray Society, address the Chairman of the Executive Council, Dr. E. F. Van Epps, Duke University, Durham, North Carolina 27706.

For information regarding the program of the annual meeting of the American Roentgen Ray Society, address the President-Elect, Dr. James C. Cook, LL 14 Professional Plaza, 3790 Woodward Avenue, Detroit, Michigan 48201.

For information regarding membership in the American Radium Society, address the Secretary, Dr. John V. Blady, The Parkway House, 2201 Benjamin Franklin Parkway, Philadelphia, Pennsylvania 19130.

For information regarding the program of the annual meeting of the American Radium Society, address the President, Dr. Juan A. del Regato, Penrose Cancer Hospital, 2215 North Cascade Avenue, Colorado Springs, Colorado 80907.

THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE is owned, maintained by, and in the interests of the American Roentgen Ray Society, Inc. It is issued monthly by Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Illinois 62703. THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE does not hold itself responsible for any statements made or opinions expressed by any contributors in any article published in its columns.

Delivery is not guaranteed. Replacements are not guaranteed nor promised, but will be attempted if extra single copies are available and only if requested within 30 days from first of month following publication (17th of month) for domestic subscribers and 60 days for foreign subscribers.

Annual subscription price is as follows: United States, U. S. Possessions, U. S. Trusteeships, Pan-American Union, and Canada, $20.00; other countries $22.00. Prices for back volumes quoted on application. Extra single copies of back issues, if available, $2.00, postpaid. Current subscriptions may begin with any issue. Remittance should be sent to CHARLES C THOMAS, PUBLISHER, 301–327 East Lawrence Avenue, Springfield, Illinois 62703, U.S.A.

ADDRESS CHANGE—When a change of address is necessary please allow at least 60 days notice and preferably 90 days. When ordering a change of address, send the Publisher both the old and new address.

Entered as Second-class at Springfield, Illinois under the Act of March 3, 1879. Printed in U.S.A.
Second-class postage paid at Springfield, Illinois and at additional mailing offices.

Copyright © 1969, by AMERICAN ROENTGEN RAY SOCIETY, Inc. No part may be duplicated or reproduced without permission of both the Publisher and the Editor.

THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE

VOL. 105 FEBRUARY, 1969 NO. 2

TABLE OF CONTENTS

The Lung: The Challenge of Nuclear Medicine. JAMES LELAND QUINN, III 251
Precise Alignment of X-ray Beams for Stereotactic Surgery. PAUL C. HODGES, M.D., AND FRANCISCO GARCIA-BENGOCHEA, M.D. 260
An Image Enlargement Scale for Stereotactic Surgery. EDWIN M. TODD, M.D., AND BENJAMIN L. CRUE, JR., M.D. 270
Stereotaxic Transsphenoidal Biopsy and Cryosurgery of Pituitary Tumors. ROBERT W. RAND, PH.D., M.D., GUNNAR HEUSER, PH.D., M.D., ALFRED DASHE, M.D., DONALD ADAMS, M.D., AND NATHAN ROTH, M.D. 273
Localization of the Calcified Pineal Body on Lateral Roentgenograms. CAPTAIN RONALD P. PAWL, MC, USA, AND CAPTAIN ARTHUR K. WALTER, MC, USA 287
Suprasellar Subarachnoid Cysts. ANDRÉ SANSREGRET, M.D., ROGER LEDOUX, M.D., FERNAND DUPLANTIS, M.D., CHRISTIAN LAMOUREUX, M.D., ALCIDE CHAPDELAINE, M.D., AND PIERRE LEBLANC, M.D. . 291
Congenital Arachnoid Cysts. YAHYA M. BERKMEN, M.D., JACK BRUCHER, M.D., AND JAMES H. SALMON, M.D. 298
Post-Traumatic Leptomeningeal Cysts. FRANK H. GRUBER, M.D. . . . 305
Cartilaginous Tumors of the Base of Skull. HIDEYO MINAGI, M.D., AND THOMAS H. NEWTON, M.D. 308
The Calvarial "Doughnut Lesion": A Previously Undescribed Entity. THEODORE E. KEATS, M.D., AND JOHN F. HOLT, M.D. 314
Calvarial Bone Defects in Neurofibromatosis: A Case Report. M. M. SAHA, K. N. AGARWAL, AND O. P. BHARDWAJ 319
Sarcoidosis of the Skull; Report of a Case. OSCAR A. TURNER, M.D., AND SANFORD R. WEISS, M.D. 322
An Unusual Angiographic Appearance of Cerebral Arteriovenous Malformations. LTC WILLIAM M. HAMMON, MC, USA 326
Aneurysms of the Superficial Temporal Artery. CHARLES B. WILSON, M.D. 331
Posterior Fossa Aneurysms Presenting As Mass Lesions. H. F. W. PRIBRAM, M.D., D.M.R.D., J. D. HUDSON, M.D., AND ROBERT J. JOYNT, M.D. 334
Vascular Malformations of the Posterior Fossa Including the Tentorial Hiatus. LAWRENCE H. ZINGESSER, M.D., MANNIE M. SCHECHTER, M.D., E. LEON KIER, M.D., AND MARK S. O'BRIEN, M.D. 341
Selective Third Ventricular Catheterization for Pantopaque Ventriculography. HAROLD A. WILKINSON, M.D. 348

(Continued on page iv)

Idiopathic Familial Cerebrovascular Ferrocalcinosis (Fahr's Disease) and Review of Differential Diagnosis of Intracranial Calcification in Children. DONALD P. BABBITT, M.D., T. TANG, M.D., J. DOBBS, M.D., AND R. BERK, M.D. 352

Autotomography Applied to the Pharynx and Dens; A Simple Wand for the Technique. EDWIN L. LAME, M.D., AND THOMAS J. REDICK . . . 359

Roentgenographic Examination of Foramen Transversarium of Axis; Practical Considerations. TRYGVE O. GABRIELSEN 361

Calcification of the Posterior Longitudinal Ligament: A Cause of Cervical Myelopathy. HIDEYO MINAGI, M.D., AND ARTHUR T. GRONNER, M.D. 365

Roentgenographic Correlations in Cervical Spondylosis. H. A. WILKINSON, M.D., M. L. LEMAY, M.D., AND E. J. FERRIS, M.D. 370

The Neurologic Complications of Paget's Disease in the Cervical Spine. FRIEDA FELDMAN, M.D., AND WILLIAM B. SEAMAN, M.D. . . . 375

Spontaneous Epidural Spinal Hemorrhage. MARTIN E. HARRIS, M.D. . . 383

Intraspinal Dermoids and Epidermoids. S. K. GUPTA, M.D., D.M.R., AND Y. P. BHANDARI, M.D., D.M.R.E. 386

The Occult Intrasacral Meningocele. IRVING S. YOUNG, M.D., AND ANDRÉ J. BRUWER, M.D. 390

Schistosomiasis of the Spinal Cord. ARNOLD CHAIT, M.D., AND WILLIAM E. GANNON, M.D. 400

Effect of Parabens on the Permeability of the Blood: Brain Barrier to Water-Soluble Radiopaque Media. WILLIAM H. STRAIN, PH.D., ROBERT J. RIVERS, JR., M.D., RICHARD J. O'REILLY, M.D., DANIEL T. DANAHY, M.D., MARTIN R. THOMAS, M.D., AND ROBERT M. WILSON . . . 404

A Simple Biplane Myelographic Table. H. F. W. PRIBRAM, M.D., D.M.R.D., R. E. KITCHEN, B.S.E.E., AND M. P. NEAL, JR. M.D. 411

Ultrasonic Diagnosis of Subdural Hematomas. JEFFREY ROTHMAN, M.D., STANLEY SHATSKY, B.S., IRVIN KRICHEFF, M.D., AND NORMAN CHASE, M.D. 413

B-Scan Ultrasound Exploration of Neoplastic Disease. BRUNO DAMASCELLI, M.D., FRANCA FOSSATI, M.D., TITO LIVRAGHI, M.D., AND ALDO SEVERINI, M.D. 428

Echographic Diagnosis of Retroperitoneal Lymph Node Enlargement; Ultrasound Scanning Technique and Diagnostic Findings. W. MICHAEL ASHER, M.D., AND ATIS K. FREIMANIS, M.D. 438

A Modified Technique of Ultrasonography for the Detection and Differential Diagnosis of Breast Lesions. FRANK H. DELAND. 446

Officers 453

Editorials

Who Should Do Echography? ATIS K. FREIMANIS, M.D. 454

W. Walter Wasson, M.D., 1884–1968. WENDELL G. SCOTT, M.D. . 456

News Items 459

Book Reviews 462

Books Received 463

Society Proceedings 465

Abstracts of Radiological Literature 471

"prep" the colon with pleasant-tasting X-PREP Liquid

(standardized extract of senna fruit)

Specifically designed for preradiographic bowel evacuation, X-PREP Liquid permits excellent visualization in G.I. and urologic roentgenography.

No significant gas shadows. No residual oil droplets.

X-PREP Liquid reduces or eliminates the need for enemas prior to radiography.

And delicious X-PREP Liquid gives a welcome reprieve for your patients from the obnoxious taste of castor oil.

Easy-to-take, X-PREP Liquid is also easy to administer. Premixed and premeasured, this effective bowel evacuant comes in small, single-dose bottles—to be taken between 2 and 4 p.m. on the day prior to radiography. Patients should be advised to expect strong purgative action.

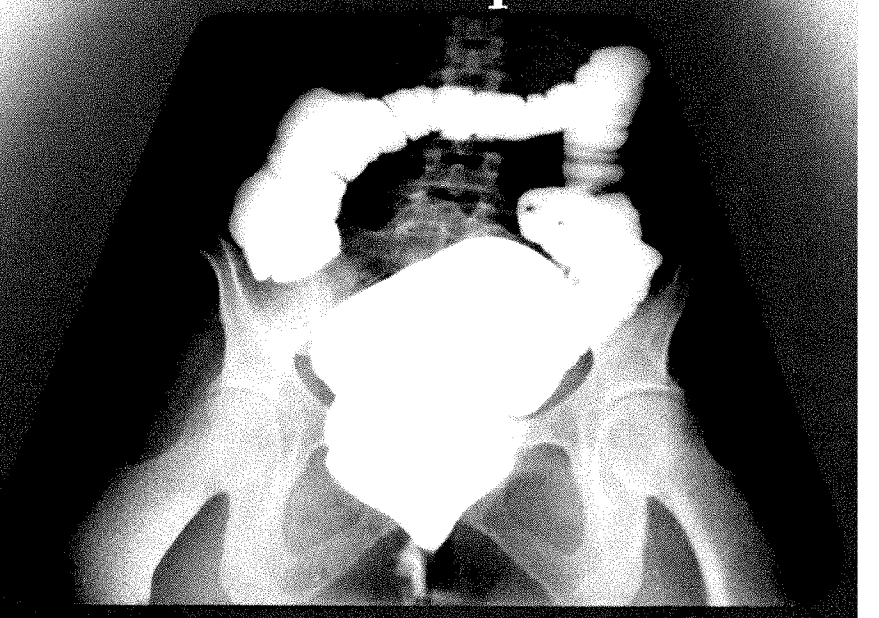
Contraindication: Acute surgical abdomen.
Supplied: Ready-to-drink in 2½ oz. bottles (complete adult dose).
Also available: X-PREP Powder (standardized senna concentrate). Mixed with water, ¾ oz. canister provides complete adult dose.

GRAY PHARMACEUTICAL CO., AFFILIATE,
THE PURDUE FREDERICK COMPANY,
Yonkers, New York

© COPYRIGHT 1968, GRAY PHARMACEUTICAL CO. E-23168R



for a clear picture



X-ray visualization following barium enema. Patient prepared with single dose of X-PREP Liquid—2½ oz. Note absence of fecal retention. Courtesy of Statman, A. J.: An Effective Single-Dose Evacuant, J. M. Soc. New Jersey 63:95 (March) 1966.

YOU ARE LOOKING AT THE ONLY RADIATION DOSIMETRY SYSTEM THAT CAN MEASURE ANY TLD PHOSPHOR OR DOSIMETER.



No matter what shape, size or type your dosimeter is, the Model 7100 Thermoluminescence Dosimetry Readout Instrument, with a dose range from 10^{-4} to 10^{6} rads, can measure it.

The basis for this versatility in measurement capability is reusable and exchangeable heating elements with a removable planchette for measuring any shape of dosimeter and loose powder, too.

Although all other TLD phosphors can be measured by the Model 7100 TLD system, ISOTOPES exclusive, patented Lif-Teflon dosimeters in disc, rod and tape form offer several distinct advantages. They are strong, mechanically flexible, easily handled, and combine the desirable physical-chemical properties of Teflon with the excellent thermoluminescent properties of LiF.

The new ISOTOPES Con-Rad TLD Readout Instrument combined with its accessories and a variety of LiF-Teflon dosimeters constitutes the most versatile and thoroughly proven TLD system available. It is backed by thorough technical support, consultative assistance and the benefits of our continuing program of research.

To learn more about the new Model 7100 TLD system, write Laboratory Products Division, ISOTOPES, 50 Van Buren Avenue, Westwood, New Jersey 07675. (West Coast: 4062 Fabian St., Palo Alto, California 94303) U.S.A.

ISOTOPES

A TELEDYNE COMPANY

Roenten®



The preferred bowel evacuant — senna, purified and biologica assayed.

Clinical studies, based on 385 in-patients and 105 out-patier establish the efficiency and safety of Roenten as a bowel evacu prior to x-ray.

A Choice in Cleansing Strength to Meet Variable Patient Cont

2-Gram Strength

Roenten® 2

Contains 2 grams of the active ingredient Senna (Cassia angustifolia) per 30 gram (1 oz.) dose. Found by Reavis, et al[1] to be comparable to castor oil in effectiveness as a bowel cleansing agent for radiography under **hospital control conditions.**

[1]Reavis, Charles W., et al, RADIOLOGY, Vol. 76, No. 4, Pages 642-643, April 1961



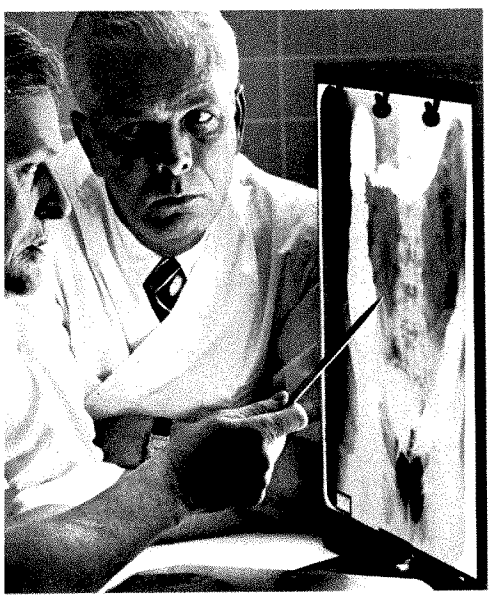


3-Gram Streng

Roenten®

Contains 3 grams of the acti gredient Senna (Cassia angust per 30 gram (1 oz.) dose fo more difficult cleansing pro and variable control conditions

DEPENDABLE



DEPENDABILITY: The preferred bowel evacuant, senna, purified and biologically assayed — in suspension assures rapid and complete bowel evacuation. Incidence of continuing spasm reduced.

Purified and Biologically Assayed, Cassia Angustifolia Senna Leaflets Blended with Agreeable Flavoring Agents.

Usual Dosage Directions

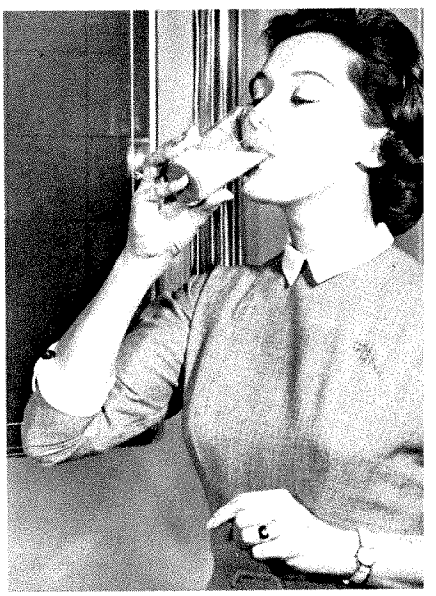
Contents of one container (30 Grams) stirred into three-quarters glass of milk or water, as physician directs, to make a readily acceptable drink which is the adult dose. Children take proportionately less as directed by the physician. When used to prepare for diagnostic X-ray it is taken at 4 or 7 P. M. (NO SUPPER) of the preceding day as directed.

CAUTION: Not to be used when abdominal pain, nausea, vomiting or other symptoms of appendicitis are present.

IMPORTANT: Frequent or prolonged use of this preparation may result in dependence on laxatives.

Samples for clinical evaluation supplied on request.

ACCEPTABLE

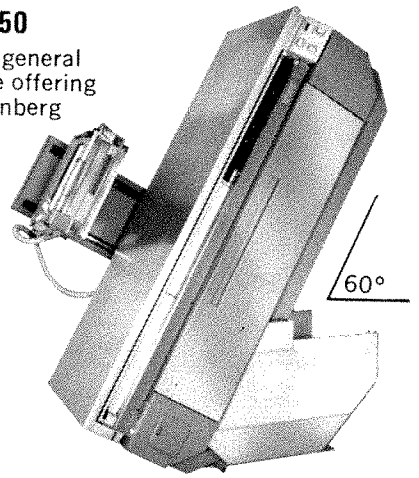


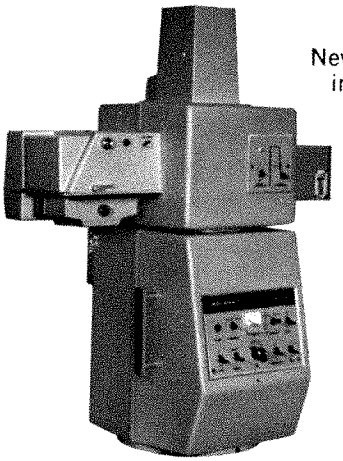
ACCEPTABILITY: The contents of one 30 gram c (1 oz.) stirred in ¾ glass of water or milk as yo makes an attractive, really pleasant tasting, c flavored non-oily suspension — invites the patient the full dose.

Brayten PHARMACEUTICAL CO.
Division of Chattem Drug & Chemical Company
1715 W. 38th St., Chattanooga, Tenn. 37409

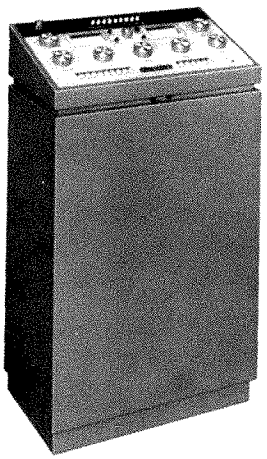
New and improved products... expanded technical support

WINDSOR 150
An improved general purpose table offering 60° Trendelenberg



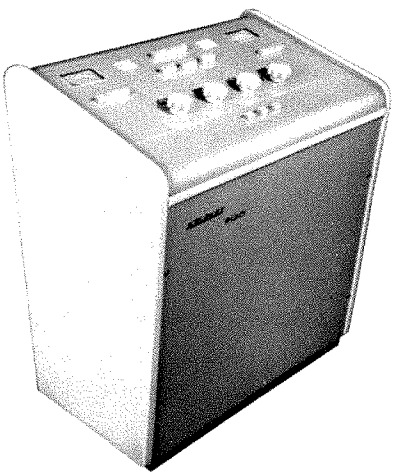


SCAT V
New optical design for image enhancement

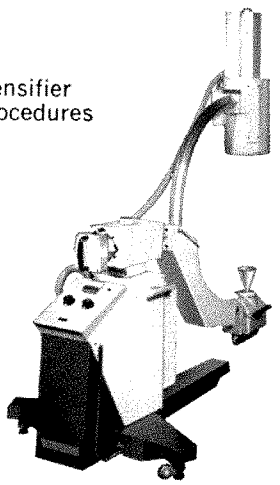


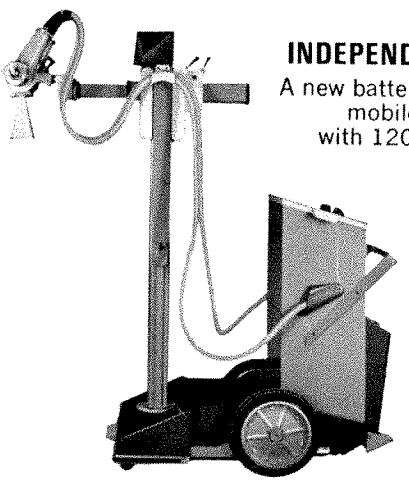
HARLECH
The high powered x-ray generators with solid state and integrated circuitry

3-PHASE
X-RAY GENERATORS
in 700 and 1000 MA capacities



CYCLOPE
A new mobile TV intensifier system for special procedures

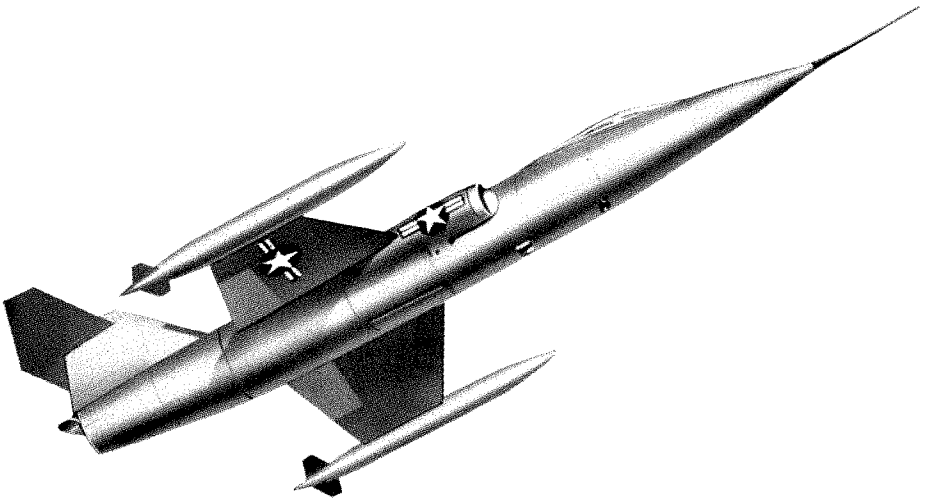




INDEPENDENT "TC"
A new battery operated mobile x-ray unit with 120 KV output

KELEKET CGR

WALTHAM, MASSACHUSETTS 02154



Fastest X-Ray screens made. Rādelin® STF-2

Radelin STF-2's are the fastest X-ray screens made, and they've been the fastest for years.

STF-2's are at least 30% faster than your present high speed screens. Their resolution provides excellent definition even at STF-2's extremely high speed; makes them ideal for high Kv, portable, spot film and roll film technics as well as for routine radiography — minimizing patient exposure.

Get speed, clarity and durability. Go with the best; Radelin STF-2. The fastest X-ray screen you can buy.

USR

RĀDELIN MEDICAL PRODUCTS
UNITED STATES RADIUM CORPORATION
MORRISTOWN, NEW JERSEY 07960

A step ahead in

For two decades, B-D has seen medical progress demand more and more skilled work from relatively fewer skilled hands.

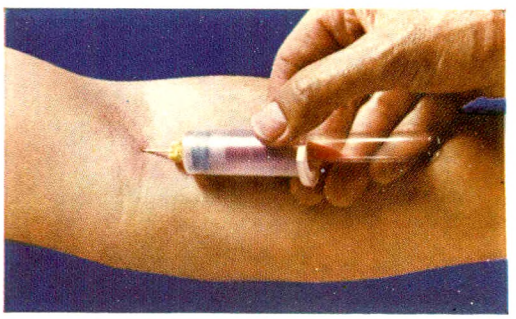
We can't add hands. We can't synthesize skill.



LUER-LOK Tips on PLASTIPAK Syringes prevent accidental needle separation and medication loss... yet allow easy needle detachment when required.

But we *can* help you with the chores – the thankless, routine "scutwork" that wastes the skill only you can supply.

B-D has made a science out of cutting scutwork.



Recently introduced VACUTAINER Multiple Sample Needle makes collecting multiple blood specimens easier and faster without leakage.

We study the jobs you do and the materials you use. We look for the repetitive, time-consuming steps in skilled procedures. For sources of risk, error or uncertainty. For areas of needless discomfort.

We'll put a dozen engineers to work studying the bevels of a needle or a means for its safe, easy destruction after use.

We analyze. Simplify. Improve. And innovate.

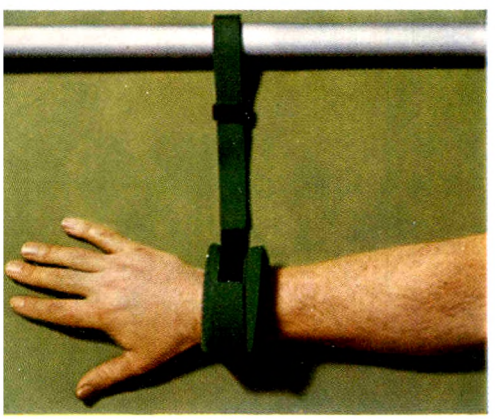
The B-D name is a synonym for half a hundred practical advances

patient care.

ı hospital and laboratory tech-
iques. Like needles with specially
ngled side bevels for consistent
ıarpness. Syringes with a positive
ɔck that prevents accidental
eedle separation. A blood-collect-
ıg system that's as flexible as it is
unctional.

And disposability.

When we can't take a giant step,
ve take little ones. Carefully con-



Newly designed ACE Limb Holder provides sure, safe, gentle immobilization of arms or legs with complete comfort for the patient. Easily and rapidly applied and released... with no buckles or leather straps.



ASEPTO Tab-Top Thermometers are universally recognized for accuracy and use-tested design...color-coded for instant recognition.

trolled steps, with infinite attention to detail. Always in the same direction. Always aimed at freeing skilled hands from needless routine...at making it easier for you to use your skill to the fullest.

That's why everything changes at B-D but our name.

BECTON-DICKINSON
Rutherford, New Jersey 07070
Division of Becton, Dickinson and Company

ACE, ASEPTO, B-D, LUER-LOK, PLASTIPAK AND VACUTAINER ARE TRADEMARKS
39769

B-D

A step ahead in patient care.

Improved reliability, even better performance.

Ohio Nuclear's new Model 84FD Dual Five, is the only scanner employing reliable, digital logic, computer-type electronics.

Speeds up to 750 cm./minute produce simultaneous, opposed view photoscans in less than half the time required by other scanners.

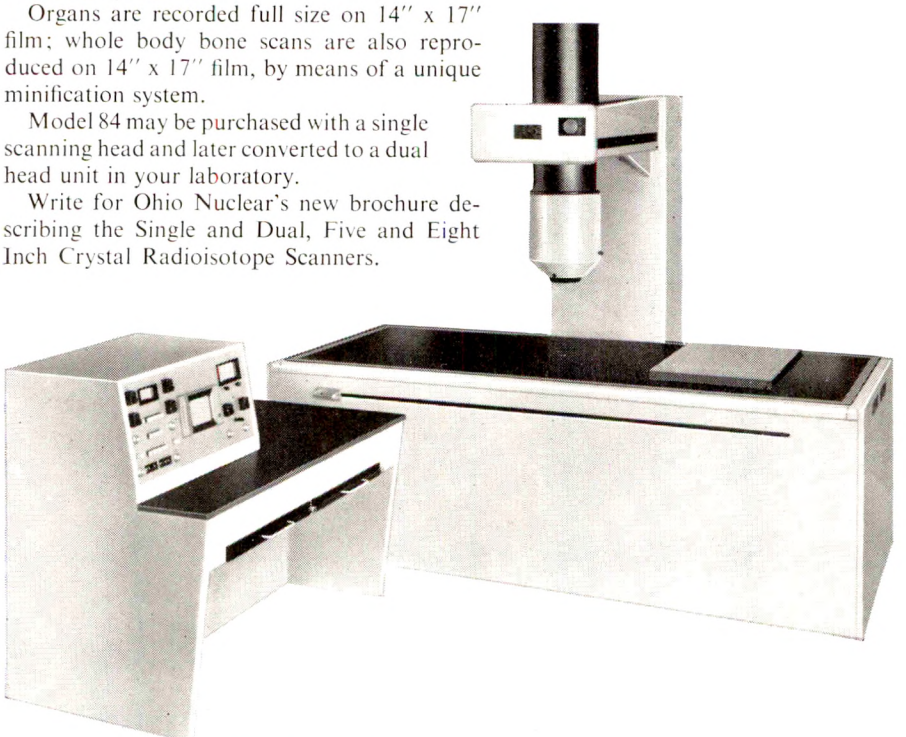
Scan progress is visually monitored on a storage cathode ray tube, which retains the organ image until manually erased.

Simplified pushbutton controls are conveniently located on the desk console. Photo Intensity Computer (PIC) circuit provides consistent, comparable maximum film density at the push of a button. Selectable levels of contrast enhancement and background erase accommodate individual preference.

Organs are recorded full size on 14″ x 17″ film; whole body bone scans are also reproduced on 14″ x 17″ film, by means of a unique minification system.

Model 84 may be purchased with a single scanning head and later converted to a dual head unit in your laboratory.

Write for Ohio Nuclear's new brochure describing the Single and Dual, Five and Eight Inch Crystal Radioisotope Scanners.



ohio-nuclear, inc.

1725 Fall Avenue, Cleveland, Ohio 44113 (216) 621-8142

SQUIBB

a research concept in contrast visualization

for clear definition of disease:

this oral medium is the message . . .

Oragrafin® Calcium (Squibb Calcium Ipodate) visualizes the gallbladder and ducts quickly and clearly with few undesirable reactions. For rapid or routine studies of the gallbladder and biliary ducts, Oragrafin permits efficient absorption for maximum concentration and excellent contrast—with bowel residue in only a small percentage of patients and few patient problems.

Oragrafin (Squibb Ipodate) in radiography — an advanced medium of biomedical communication. According to McLuhan's[1] provocative new theories of communications, all media are considered "extensions of man"—the means by which he extends his understanding and control of the universe and himself. In biomedical communications, where man monitors the diverse processes of molecular and cellular change, modern contrast radiography is an advanced medium.

Today, in cholangiography and cholecystography, as the medium becomes increasingly oral, the diagnostic message is clear, rapid, and convenient with Oragrafin (Squibb Ipodate).

For summary of contraindications, precautions, and side effects, see end of this advertisement.



the medium:
Oragrafin®
Squibb Ipodate
the message:
maximum concentration... excellent toleration

high absorption index—"No one will dispute the statement that the diagnostic reliability of oral cholecystography depends upon the degree of absorption of the contrast medium employed."[2] Radioisotope studies with ipodate sodium show a markedly improved absorption index (approximately 70 per cent) with no increase in the toxic properties.[2]

excellent opacification—"In addition to its ease of administration and safety, its principal advantages are a high yield of diagnostic films...."[3]

less bowel residue—"Incomplete and variable absorption of a cholecystographic agent is not desirable, for the opacification of the gallbladder is then less dependent on the status of the gallbladder and more a reflection of the percentage absorption."[4]

"Opaque material in the bowel was found in 46 per cent of [105 patients in] the...[iopanoic acid] group as compared with 9 per cent of those [99] of the [Oragrafin Sodium Capsules]...group."[4] In another study, 49 of 100 patients receiving iopanoic acid had residue in the gastrointestinal tract, while only 15 of 100 patients receiving Oragrafin Sodium Capsules had such residue.[5]

no evidence of nephrotoxicity, infrequent side effects—In contrast to findings with other cholecystographic agents, Lewitan and Garcia[6] reported in their 246-patient study: "With ipodate calcium... there was no clinical evidence of immediate or delayed nephrotoxicity in any of the patients given it...."[6] To study possible renal toxicity, "Creatinine clearance tests were also done before and after administration of multiple doses in excess of 6 gm. in 8 cases, and showed no significant alterations."[6] However, "Multiple doses beyond 6 gm. are not recommended."[6]

In their study of 120 patients, Glenn and O'Brien reported "...no reactions in this series of patients attributable to the administration of [Oragrafin]...."[3]

And, McCrory reported that Oragrafin Sodium and Calcium was "...used routinely in cholecystographic studies in approximately 2000 patients with excellent diagnostic films and only rare and mild reactions."[7]

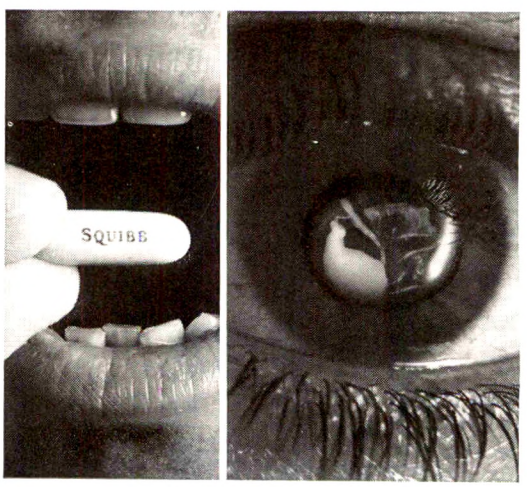
fewer side effects than iopanoic acid—According to White and Fischer,[4] 36 (36.4%) instances of side effects occurred in 99 cases with Oragrafin Sodium, 3 Gm. compared with 87 (82.9%) in 105 cases with iopanoic acid, 3 Gm. Kinds of side effects noted were nausea, vomiting, diarrhea, cramps and dysuria—all less frequent with Oragrafin Sodium (Squibb Sodium Ipodate).

Juhl,[5] in his study of 200 patients (100 on iopanoic acid and 100 on sodium ipodate), found that the incidence of nausea and vomiting was equal in the two groups.[5]

Oragrafin (Squibb Ipodate) dosage schedules Oragrafin (calcium or sodium ipodate) permits overnight cholecystography and cholangiography.

	Gallbladder Films		Films of the Gallbladder and Biliary Ducts
11 P.M.	6 Capsules OR (or 12 Capsules)	1 packet of Granules (or 2 packets)	6 Capsules (or 1 packet of Granules, if preferred) and
next morning 8 A.M.			1 packet of Granules
9 A.M.	Visualization of gallbladder	Visualization of gallbladder	Visualization of ducts and gallbladder
10 A.M.			
11 A.M.			

For summary of contraindications, precautions, and side effects, see next page.



speed and convenience of Oragrafin® Calcium Granules

Squibb Calcium Ipodate

new clinical study[8] demonstrates improved diagnoses with calcium ipodate—"A group of 114 patients with poorly filled gallbladders after routine administration of iopanoic acid were given 6 gm. of [calcium] ipodate granules immediately following their routine cholecystography. In 66 per cent of these patients opacification of the gallbladders was obtained within 3 hours, allowing a definite diagnosis. Of the remaining 33 per cent, one-half were ultimately proven diseased." "It is apparent that many poorly visualized gallbladders can be rendered visible by the ingestion of ipodate granules.... A whole day may be saved and other diagnostic studies may be performed."[8]

patient convenience—Routine cholecystography night-before procedure is easy for patients to follow; palatable granules further enhance patient acceptability. Rapid clearance of medium permits same-day administration and gallbladder and ductal films, and if necessary, same-day re-examination; reduces need for I.V. studies.

rapid absorption permits same-day re-examination—To determine the cause of nonopacification after routine cholecystography using 6 capsules, physicians may require re-examination by repeating the procedure at a later date (sometimes doubling dose to 12 capsules), or by administering more agent the evening of the first unsuccessful examination (again sometimes doubling dose to 12 capsules), and repeating the study the next day. "The advantage of the calcium ipodate method is that the examination can be completed in five additional hours with a limited dose of contrast agent."[9]

"a valuable medium for peroral cholegraphy"[6]—Rapidly absorbed from the gastrointestinal tract, calcium ipodate has been reported by some investigators to be diagnostically superior to other oral cholangiographic contrast agents.[10,11] With careful timing of the examination and the use of tomograms or laminograms, the frequency of good results can approximate that obtained with intravenously administered agents.[10] According to Lewitan and Garcia,[6] the medium's relative safety makes it a valuable medium for peroral cholegraphy. Timesaving and economical Oragrafin Calcium Granules may be particularly useful in certain patients for whom I.V. radiography presents potential hazards, such as elderly patients and those with cardiovascular disease.

Unique among oral media, Oragrafin Calcium Granules permits same-day films of the gallbladder and the ductal system.

dosage schedule for films of gallbladder and ductal system

8 A.M.	2 packets of granules
9 A.M.	visualization of ducts
10 to 11 A.M.	visualization of gallbladder

Contraindications: Contraindicated for persons sensitive to oral iodine compounds or for patients with *combined* renal and hepatic disease or *severe* kidney impairment. Gastrointestinal disorders, which may interfere with absorption, or liver dysfunction, which may result in inadequate biliary secretion of medium, are likely to result in unsatisfactory visualization.

Precautions and Side Effects: Mild and transient nausea, vomiting, or diarrhea sometimes occur; but the incidence can be reduced by using the calcium granules and restricting the dosage to 3 Gm. Transient headache, dysuria, or abdominal pains may occur.

Hypersensitivity reactions may include urticaria, serum sickness-like reactions, and rarely anaphylactoid shock. They are more likely to occur in the individual with a history of allergy, asthma, hay fever, or urticaria and in the individual who is known to be hypersensitive to iodine compounds. Antihistamines and corticosteroids are used to control hypersensitivity reactions; but the occasional serious anaphylactoid reactions require the immediate use of epinephrine or phenylephrine, oxygen, and intravenous corticosteroids.

For full information see Package Insert.

Supply: The calcium salt (Oragrafin Calcium Granules) is available in single-dose foil packets providing 3 Gm. of calcium ipodate as Granules dispersed in flavored sucrose. The sodium salt is available in capsule form (Oragrafin Sodium Capsules) providing 0.5 Gm. sodium ipodate per capsule.

References: 1. McLuhan, M.: Understanding Media: The Extensions of Man, New York, McGraw-Hill Book Company, 1966. **2.** Sanen, F. J.: Amer. J. Roentgen. *88*:797 (Oct.) 1962. **3.** Glenn, J. C., Jr., and O'Brien, P. S.: Southern Med. J. *56*:167 (Feb.) 1963. **4.** White, W. W., and Fischer, H. W.: Amer. J. Roentgen. *87*:745 (April) 1962. **5.** Juhl, J. H., *et al.*: Radiology *80*:87 (Jan.) 1963. **6.** Lewitan, A., and Garcia, J. F.: Amer. J. Dig. Dis. *10*:219 (March) 1965. **7.** McCrory, E.: J. Tenn. Med. Ass. *58*:258 (Aug.) 1965. **8.** Root, H.: Amer. J. Roentgen. *101*: 621 (Nov.) 1967. **9.** Crummy, A. B.: Wisconsin Med. J. *65*:84 (Feb.) 1966. **10.** Saltzman, G. F.: Acta Radiol. *54*: 417, 1960. **11.** Ludin, H., and Lauchenauer, C.: Schweiz. Med. Wochenschr. *90*:471, 1960.

for clear definition of disease: in oral cholangiography and cholecystography

Oragrafin®

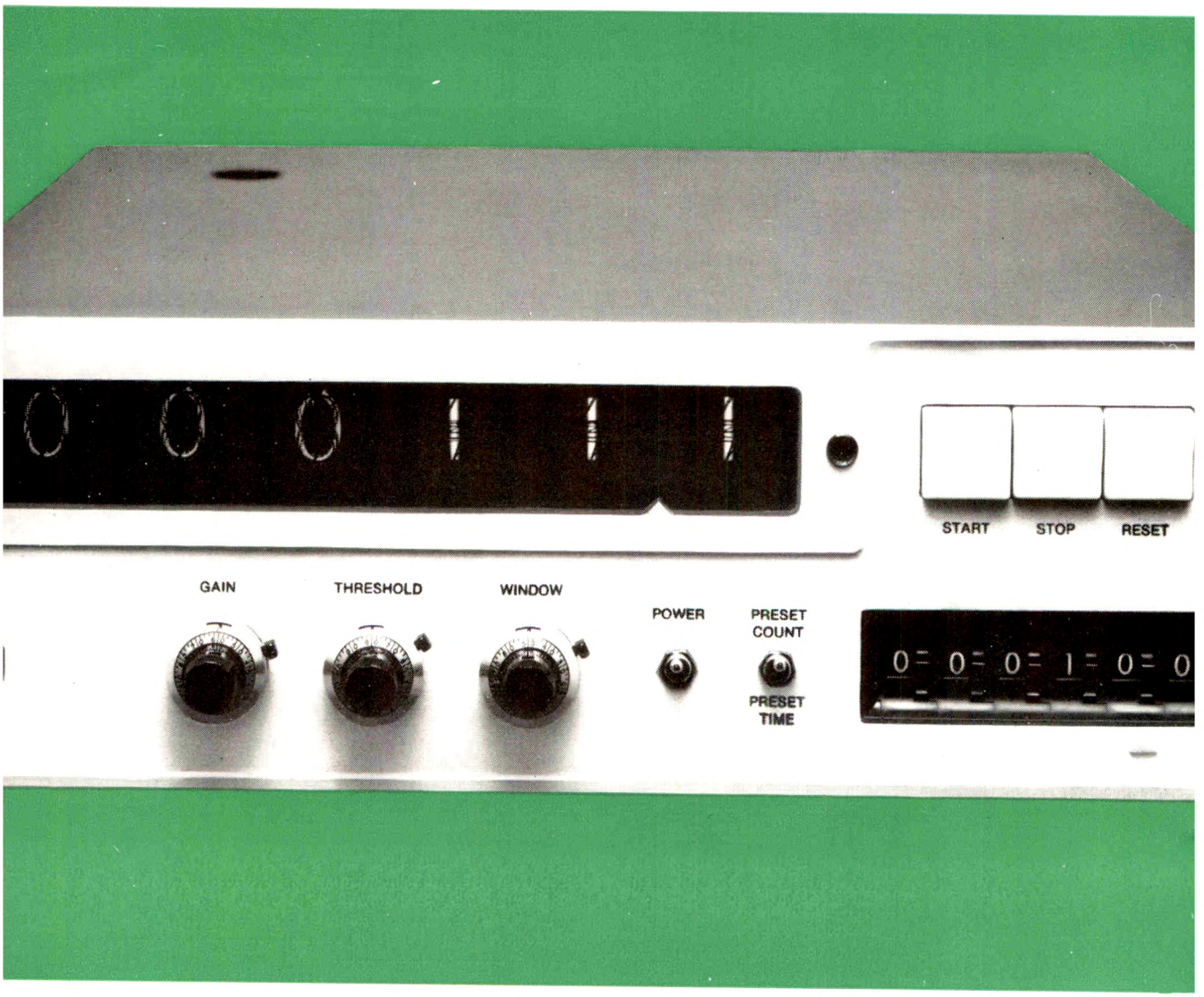
Squibb Ipodate

SQUIBB

'The Priceless Ingredient' of every product is the honor and integrity of its maker.

A 2610

Abbott Laboratories is now



This is the
LOGIC™ Well Counter–
only inches larger than this page
(12¼″ x 4 1/16″ x 13″ to be exact)

TM—TRADEMARK

in Nucl ar Instrum nts



The LOGIC Series—the most compact counting systems ever designed—is available now in 3 models.

804468

The LOGIC Counting Systems offer:

- Compactness (micrologic integrated circuitry)
- Dependability (pre-tested for 40 hours)
- Portability (25-35 lbs.)
- Versatility (choice of 3 models)
- Quality (backed by Abbott)

For more information, contact your Abbott man who knows both instruments and radio-pharmaceuticals

ABBOTT LABORATORIES NORTH CHICAGO, ILLINOIS
Abbott Laboratories, S.A., 2, rue Thalberg, 1201 Geneva, Switzerland

New directions for storage, manipulation, and analysis of data from our Pho/Gamma® III Scintillation Camera:

Now, Nuclear-Chicago makes it possible to realize even more of the clinical potential of Pho/Gamma III.

Because, information on radioisotope distribution in body organs, as visualized by Pho/Gamma III, can now be recorded—in digital form—on magnetic tape.

That's the function of our Magnetic Tape System. It consists of a multidimensional analyzer and the magnetic tape transport itself.

When connected to the Pho/Gamma III, this system permits you to record clinical data for later evaluation. And to manipulate this data at any time—to play it back, to change its mode of display, to re-record it on alternate readout devices (such as a digital printer or self-developing camera for making the familiar 15-second scintiphoto).

And, if you have access to an off-line computer, our Magnetic Tape System can be even more valuable. The data from Pho/Gamma III can be recorded in computer-compatible form and then fed into the computer (properly programmed, of course). You can thereby generate essentially automatic analysis, which can bring you entirely new insights into the organs under investigation.

The true worth of our new Magnetic Tape System can only be measured in your own work. Our job is to make Pho/Gamma III more and more versatile by making available the analytical or storage procedure you need.

Which is why, in addition to the Magnetic Tape System, we also are introducing a fast digital printer, an automatic 35-mm time-lapse camera, and a dual-channel ratemeter/dual-pen recorder as accessories for the Pho/Gamma III.

Your Nuclear-Chicago sales engineer can tell you all about Pho/Gamma III and its expanded range of accessories, including the Magnetic Tape System. Please call him. Or write directly to us. 8-237

Research in the Service of Mankind

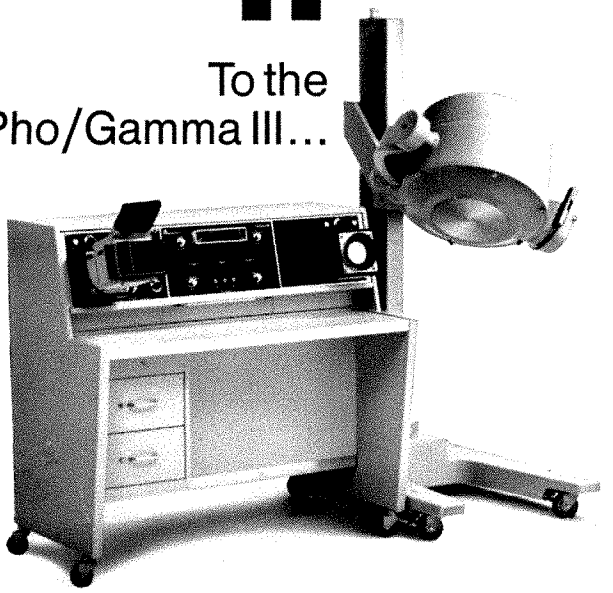
NUCLEAR-CHICAGO CORPORATION

A SUBSIDIARY OF G. D. SEARLE & CO.

307 East Howard Avenue
Des Plaines, Illinois 60018, U.S.A.
Donker Curtiusstraat 7, Amsterdam W.

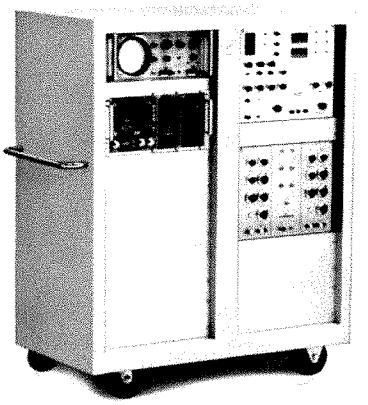
1.

To the
Pho/Gamma III...



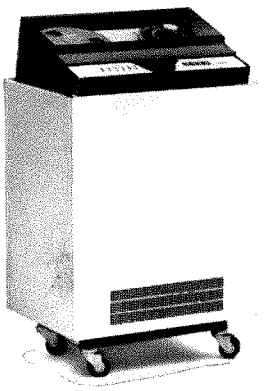
2.

Add our multidimensional
analyzer...



3.

Connect to our magnetic
tape transport, and...

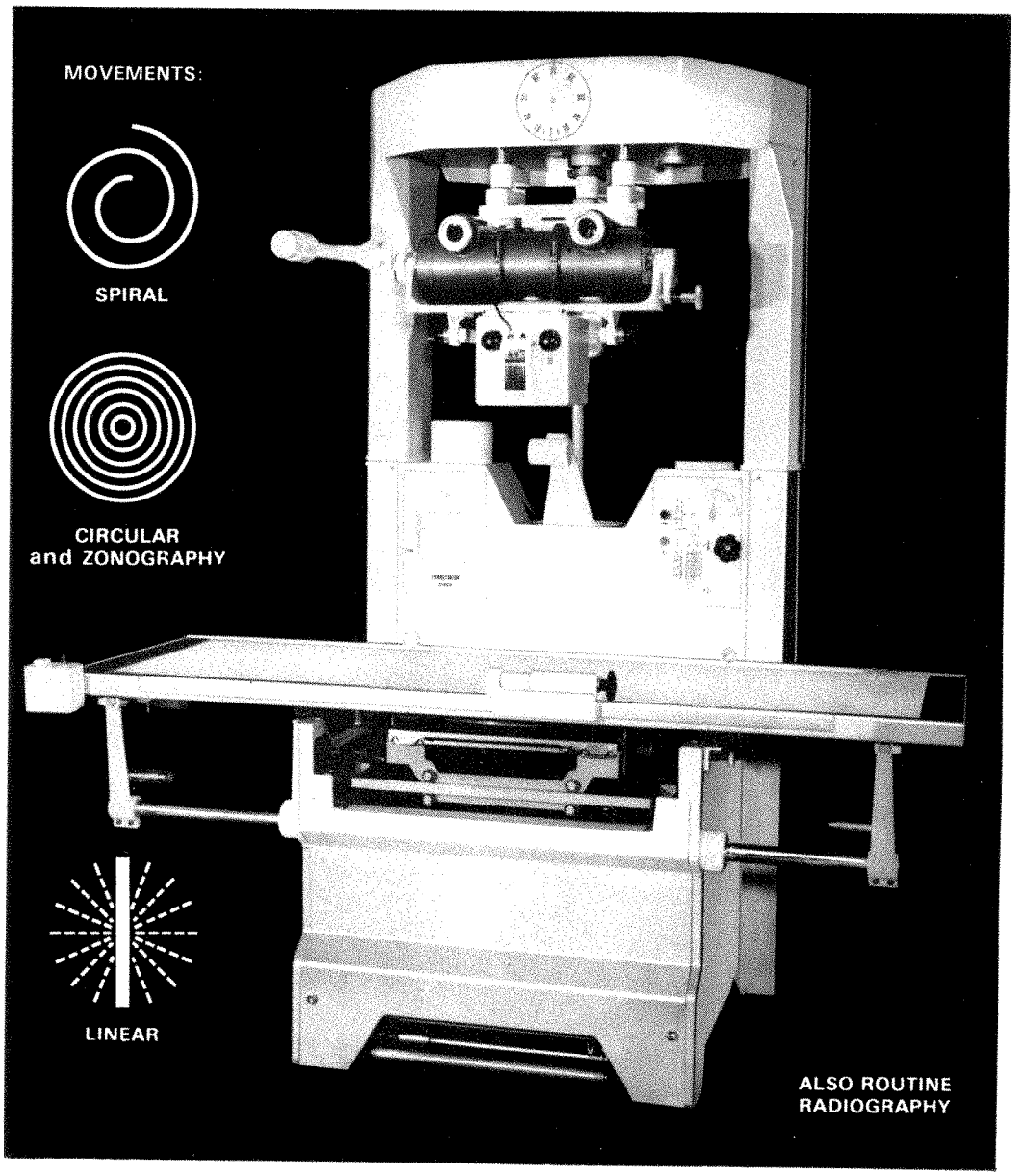


4.

Make tracks.

EUROSTRATOR

for TOMOGRAPHY...



For complete information contact your dealer or write to:

SCHICK
X-RAY

SCHICK X-RAY CO., INC.
415 Green Bay Road • Wilmette, Illinois 60091
Phone (312) 256-4700



As Ever,

We would have (if we could have) changed it to make it better—never just to make it different. But little in the past century of medical progress has suggested a compound superior to Phospho®-Soda for gentle, predictable laxative action. Rely on it for freedom from urgency, griping, irritation, or nausea. For use in almost any age group. Available regular or flavored.
Warning: Do not use when nausea, vomiting or abdominal pain is present. Frequent or prolonged use of this preparation may result in dependence on laxatives.

Phospho®-Soda

Buffered Laxative

1869-1969

Fleet® pharmaceuticals
A century of service to medicine



F38A68

C. B. FLEET CO., INC., Lynchburg, Va. 24505

The Slippery One.

There are lots of overhead tube conveyers around today. But not like this one. Go ahead, try it. Pull it all the way down. Take a finger and raise it back. Walk it around.

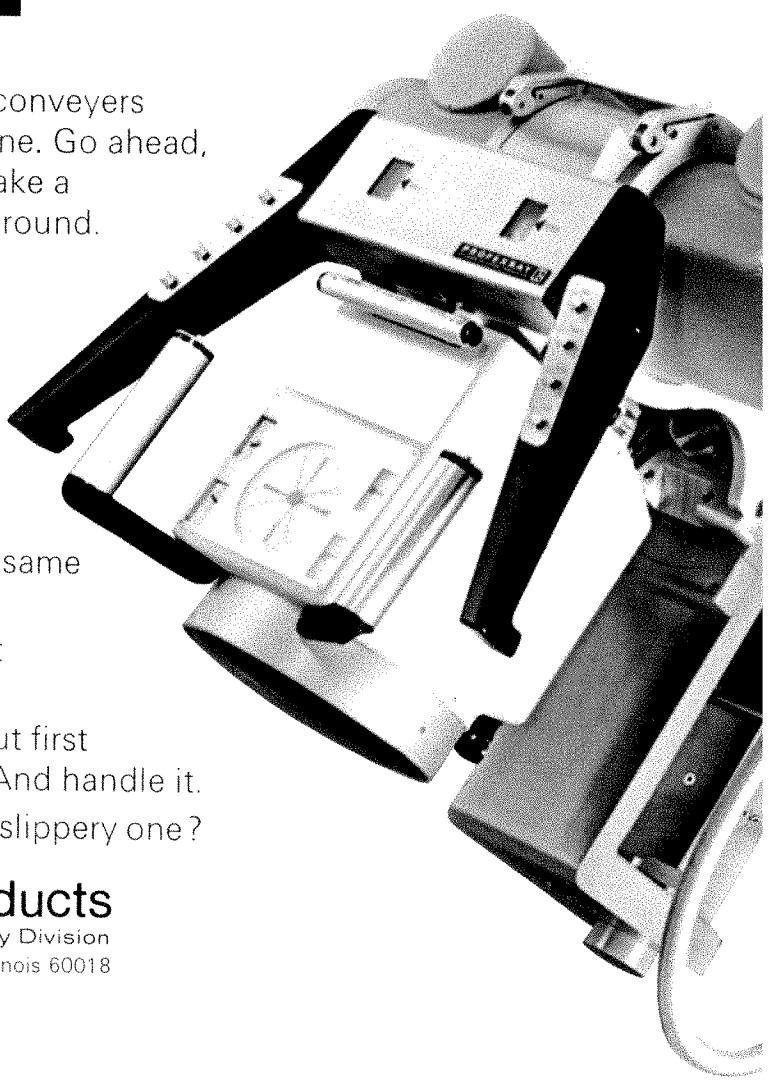
See? Not a hitch.

That's why we call it the slippery one. Because these mechanisms have been perfected. Then polished. Then perfected again. Until working with them is not just satisfactory—but satisfying. The same as with all Profexray equipment.

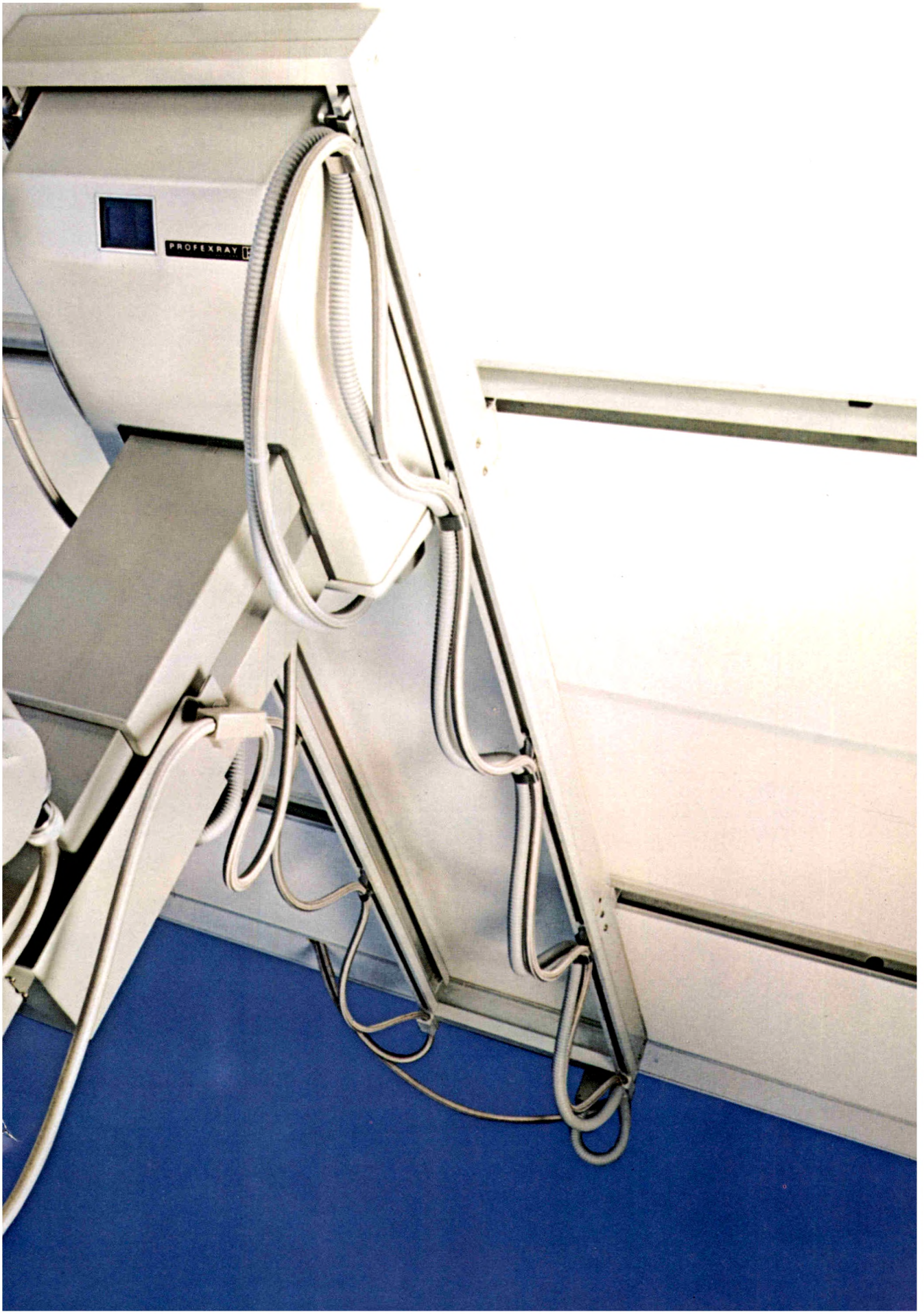
We think that makes our product better than anybody's.

We'd like you to think so, too. But first you'll have to see it. And feel it. And handle it.

How soon can we show you our slippery one?



Litton Medical Products
A Litton Industries Group, Profexray Division
515 East Touhy Avenue—Des Plaines, Illinois 60018


PROFEXRAY

16 ANSWERS TO YOUR PROBLEMS IN ROENTGENOLOGY

Offering New Techniques . . . New Procedures

☐ **MEDICAL RADIOGRAPHIC TECHNIC** (3rd Ed., 2nd Ptg.). *Rewritten by* **William L. Bloom, Jr., John L. Hollenbach,** *and* **James A Morgan,** *all of the Technical Service X-Ray Dept., General Electric Company, Milwaukee.* '67, 368 pp. (7 × 10), 510 il., 7 tables, $11.00

☐ **SELECTIVE RENAL ARTERIOGRAPHY: Its Application to the Diagnosis of Renal Vascular and Parenchymal Lesions** *by* **Ivan L. Bunnell,** *State Univ. of New York at Buffalo.* '68, 248 pp. (6¾ × 9¾), 183 il., $18.75

☐ **PRINCIPLES OF RADIOGRAPHIC EXPOSURE AND PROCESSING** (2nd Ed., 5th Ptg.) *by* **Arthur Fuchs,** *Rochester, N.Y.* '68, 304 pp. (7 × 10), 600 il., $11.00

☐ **ROENTGENOGRAPHIC DIAGNOSIS OF BLADDER TUMORS** *by* **Erich K. Lang,** *Methodist Hosp., Indianapolis.* '68, 132 pp. (7 × 10), 94 il., 11 tables, $9.75

☐ **RADIOLOGY AS AN ART AND OTHER ESSAYS** *by* **John L. McClenahan,** *Hosp. of the Univ. of Pennsylvania, Philadelphia.* '67, 104 pp., 3 il., $5.75

☐ **AIDS TO ETHICS AND PROFESSIONAL CONDUCT FOR STUDENT RADIOLOGIC TECHNOLOGISTS** (2nd Ed.) *by* **James Ohnysty,** *Saint Francis Hosp., Colorado Springs.* '68, 172 pp., $6.75

☐ **SOLITARY METASTASES** *by* **Philip Rubin,** *Univ. of Rochester Medical Center, New York, and* **Jerold Green,** *Zellerbach Saroni Tumor Institute, Mount Zion Hosp., San Francisco.* '68, 268 pp., 153 il., 30 tables, $14.75

☐ **LUNG CALCIFICATIONS IN X-ray Diagnosis** *by* **Emanuel Salzman,** *Univ. of Colorado School of Medicine, Denver.* '68, 132 pp. (6¾ × 9¾), 74 il., $7.50

☐ **ILLUSTRATIVE CRANIAL NEURORADIOLOGY** *by* **Alfred L. Schmitz,** *Univ. of California, Los Angeles;* **Samuel B. Haveson,** *Univ. of Southern California, Los Angeles; and* **Duke Hanna,** *Freeman Memorial Hosp., Inglewood.* '67, 404 pp. (8½ × 11), 532 il. (1 in full color), $31.50

☐ **THE FUNDAMENTALS OF X-RAY AND RADIUM PHYSICS** (4th Ed., 4th Ptg.) *by* **Joseph Selman,** *Univ. of Texas, Tyler.* '68, 498 pp., 306 il., 16 tables, $10.50

☐ **ERROR AND VARIATION IN DIAGNOSTIC RADIOLOGY** *by* **Marcus J. Smith,** *St. Vincent Hosp., Santa Fe.* '67, 208 pp., 68 il., 18 tables, $8.75

☐ **TREATMENT FOR CHROMOPHOBE ADENOMA** *by* **Hendrik J. Svien** *and* **Malcolm Y. Colby, Jr.** *Both of Univ. of Minnesota, Rochester.* '67, 116 pp. (6¾ × 9¾), 60 il., 15 tables, $7.50

☐ **NORMAL RADIOLOGICAL ANATOMY: Radiological Optics and Film Interpretation** *by* **Henry Tillier,** *Late Professor of Radiology, Algiers. Translated and edited by* **Ronan O'Rahilly,** *St. Louis Univ. School of Medicine.* '68, 400 pp., 375 figs., 3 tables, $12.50

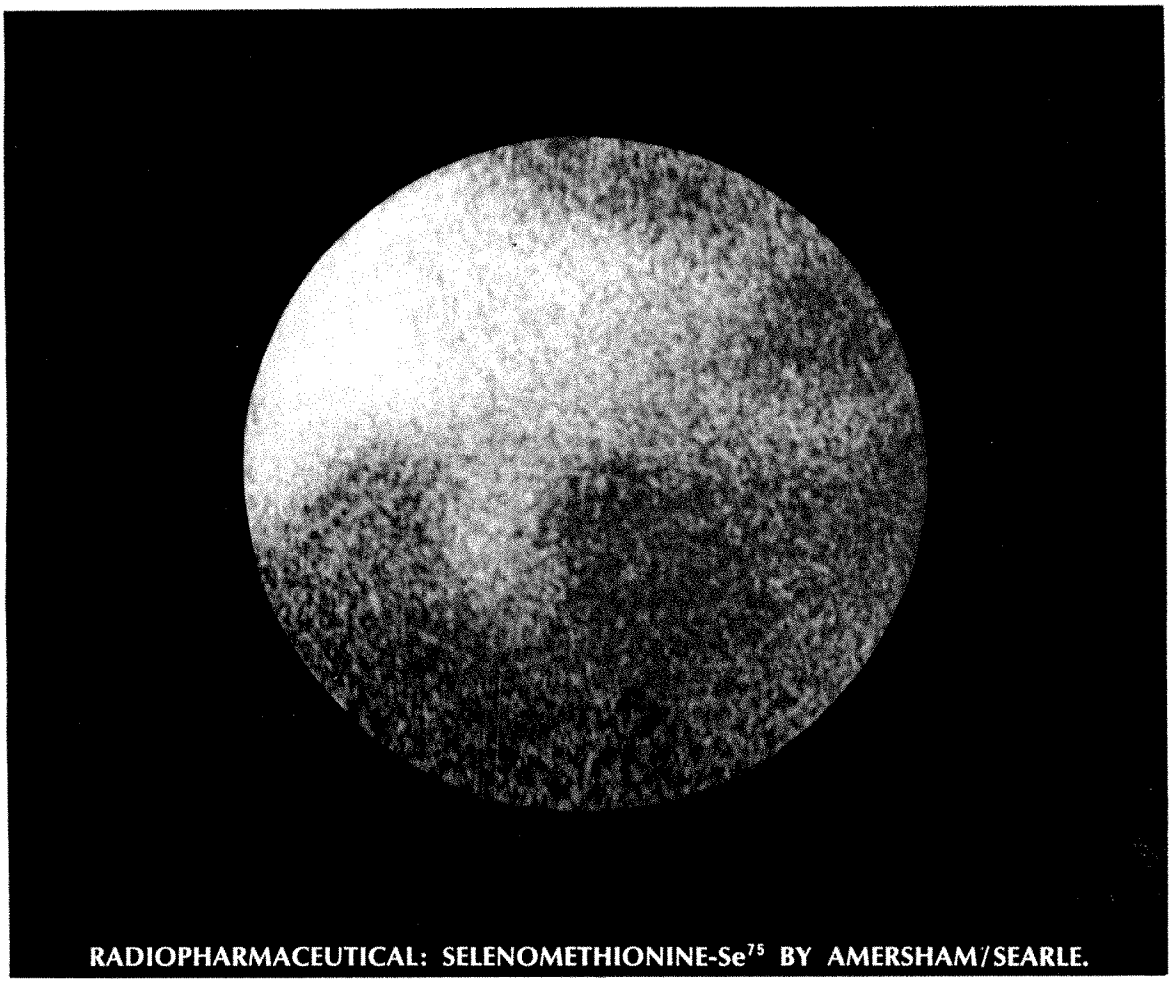
☐ **ADVANCES IN DYNAMIC RADIOACTIVE SCANNING** *compiled and edited by* **Yen Wang,** *Univ. of Pittsburgh, Pa. (10 Contributors)* '68, 140 pp., 101 il., 7 tables, $8.50

☐ **CLINICAL RADIOISOTOPE SCANNING** *by* **Yen Wang.** '67, 260 pp. (6¾ × 9¾), 280 il., 8 tables, $12.50

☐ **MAMMOGRAPHY** *by* **John N. Wolfe,** *Woman's Hosp. (Hutzel Hosp.), Detroit.* '67, 168 pp. (8½ × 11), 191 il., 25 tables, $12.50

CHARLES C THOMAS · PUBLISHER 301-327 East Lawrence Avenue **SPRINGFIELD · ILLINOIS · 62703**

Portrait of a Pancreas.



RADIOPHARMACEUTICAL: SELENOMETHIONINE-Se^{75} BY AMERSHAM/SEARLE.

There are many problems inherent in diagnosing diseases of the pancreas by standard radiographic techniques. Further, laboratory determinations are often inconclusive.

Question: Can pancreatic pathology be ruled out as a possible diagnosis short of exploratory surgery?

Answer: Amersham/Searle Corporation now offers the clinician selenomethionine-Se^{75}—a diagnostically reliable imaging agent, especially when used with the gamma scintillation camera for rapid, continuous scintiphotography.

Amersham/Searle's selenomethionine-Se^{75} is of unsurpassed purity and stability. And these qualities are vital to your selection of a drug for your patients. Here are the important specifications for selenomethionine-Se^{75} as supplied by Amersham/Searle:

Stability: Little evidence of radiation decomposition after storage for up to 4 months at room temperature in concentrations of 1 mCi/ml.

Radiochemical purity: >95%.

Chemical purity: >90%.

For further clinical, biochemical, and technical information on L-selenomethionine-Se^{75} (sterile aqueous solution) please write for *Radiopharmaceutical Bulletin RP-1*. Or call us directly.

Indications: Pancreas imaging. **Contraindications:** Radioisotopes should not be administered to patients under 18 years of age, or to pregnant or nursing women, unless invaluable diagnostic information cannot be otherwise obtained. **Precautions:** Observe appropriate radiation-safety procedures at all times. **Availability:** Sterile aqueous solution. Specific activity ranges from 1 to 6 mCi/mg. Radioactivity concentration approximately 250 μCi in 1 ml.

Scintiphoto courtesy D. Bruce Sodee, M.D., Doctors Hospital, Cleveland, Ohio.

2000 NUCLEAR DRIVE DES PLAINES, ILLINOIS 60018 TELEPHONE: (312) 296-1055

Amersham/Searle

What tank gives you the performance of an insulated stainless model... but carries an "economy" price tag?

The Halsey *non-sweating* Fiberglas Tank



- Master jacket is dense, high-impact Fiberglas. Non-sweating; won't crack or bulge.
- Smooth inner surface with widely rounded corners makes it far easier to clean than a stainless steel tank.
- Inserts are type 316 stainless steel for rapid heat exchange and high corrosion resistance.
- Towel rack included as standard equipment.

No. 318-T.....**Fiberglas tank with two 5-gallon inserts**
No. 318-T-H.....**Fiberglas tank with two 2½-gallon inserts**



• ACCESSORIES

No. 346-TV-L. Thermostatic control valve (photo at left) controls water temperature automatically; has manual lever for easy adjustment to desired temperature. Includes mixing chamber, flow control valve, check valves, vacuum breaker, replaceable filters and dial-type thermometer.

No. 347-TV-L. Same as above, but without thermometer, vacuum breaker and flow-control valve.

No. 318-TC. Overall tank cover; stainless steel.

No. 326-TC. Insert cover for 5-gallon insert; stainless steel.

No. 326-TC-H. Same as above, but for 2½-gallon insert.

No. 318-T-PB. Overflow plumbing, shut-off valve.

Through your dealer
Write for detailed literature

HALSEY X-RAY PRODUCTS, INC.
1425-37th STREET, BROOKLYN, N.Y. 11218
CHICAGO: 7321 Monticello Avenue, Skokie, Illinois 60076
LOS ANGELES: 1816 W. 8th St., Los Angeles, Calif. 90057

HALSEY

A recommended course of action for the buyer of radiopharmaceuticals:

1 **INTROSPECTION. Think for a moment. What's your prime concern when you're ready to buy radiopharmaceuticals? Purity? Stability? Availability? Service? Which of these are important to you? Sort them out. Write them down. Give them an order of importance.**

No matter what your analysis reveals, Amersham/Searle Corporation is more than likely to have the solutions. Our range of compounds is wide—from arsenic-74 to xenon-133. Imaging agents for in-vivo investigations. Compounds for in-vitro studies. All with purity and stability of the highest order. All for prompt delivery.

2 **INVESTIGATION. Next, look into the credentials of the suppliers of radiopharmaceuticals. What have they done? What are they doing—in research, in involvement with the field of nuclear medicine itself?**

When you look into Amersham/Searle, the facts are these: A company formed as a joint venture of The Radiochemical Centre, Amersham, England, and G. D. Searle & Co. An organization capable of drawing on the resources of The Centre for radiopharmaceutical research and manufacture. A manufacturer able to utilize the resources of G. D. Searle & Co., a firm long experienced in pharmaceutical research. And a resourceful enterprise capable as well of benefiting from an exchange of information with Nuclear-Chicago Corporation (a Searle subsidiary), designers and manufacturers of nuclear instrumentation.

3 **INFORMATION. Ask to see all available information on the compounds you're interested in. What does the supplier have to say about the radiopharmaceutical? How is it said?**

A Radiopharmaceutical Bulletin from Amersham/Searle is a detailed compilation of facts on every aspect of the compound offered. Clinical information. Biochemical and chemical data. Complete specifications. And extensive bibliographies. Every radiopharmaceutical we make gets the same treatment in our Bulletins.

4 **DECISION: Once you have decided on your probable source of radiopharmaceuticals, make your move. Ask for proof of performance.**

Your phone call or written request to Amersham/Searle will start things moving. We will send complete data on any radiopharmaceutical or attempt to answer any and all questions that go beyond such data. And we'll send you a list of our Telex-connected sales offices. After all, you would expect our actions to speaker louder than our words.

2000 NUCLEAR DRIVE DES PLAINES, ILLINOIS 60018 TELEPHONE: (312) 296-1055

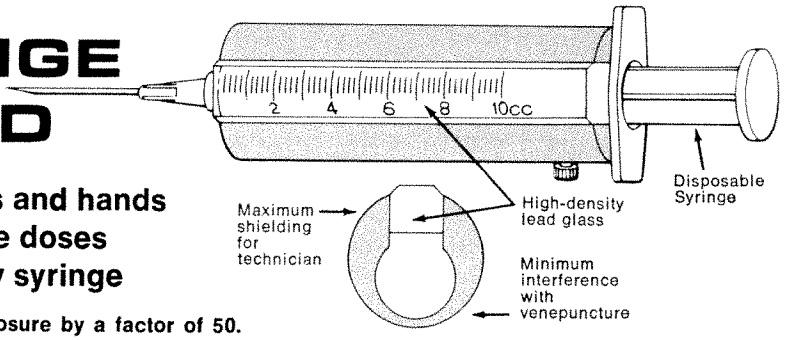


Amersham/Searle

AMERSHAM/SEARLE CORPORATION:
AN ACTIVITY OF G. D. SEARLE & CO. AND THE RADIOCHEMICAL CENTRE

8-216

NEW SYRINGE SHIELD



Protects fingers and hands from radioactive doses administered by syringe

- **Reduces Tc-99m exposure by a factor of 50.**
- **Offers maximum shielding for technician. Tapered lead wall permits minimum interference with venepuncture.**
- **Uses standard disposable syringes.**

Protect your fingers and hands from syringe-administered millicurie doses of radioisotopes ...with the new "Gamma Vue" Syringe Shield.* Whether you are working with Technetium-99m or other activities, this shield effectively reduces the ionizing radiation to tolerable limits.

For example, 8 mc of Tc-99m in an unshielded syringe wil expose your fingers and hand to a 5,000 mR/hour hazard. The "Gamma Vue" cuts this exposure by a factor of 50; I-131 dose rates are reduced 4-foid.

Consists of 3/16" lead shield with lead-glass panel for viewing the syringe calibration marks. Accepts standard disposable syringes.

56-262	Syringe Shield, 2½ cc.	$36.00
56-263	Syringe Shield, 5 cc.	$37.00
56-260	Syringe Shield, 10 cc.	$38.00
56-261	Syringe Shield, 20 cc.	$42.00

For more details, request Bulletin NM-68-C

NUCLEAR ASSOCIATES, INC.
35 URBAN AVENUE, WESTBURY, N.Y. 11590, PHONE (516) 333-9344

*Patent Pending

31 YEARS of integrity have helped us to become America's largest buyers of

USED X-RAY FILM

- We purchase all makes and sizes from any point in the nation, and pay the freight cost.
- We remit in advance if desired, or promptly after receipt and tally of the value.
- Write for prices today. We will send shipping labels and direct your film to our nearest plant.

DONALD McELROY, INC.

3201 Old Glenview Road, Wilmette, Illinois 60091
Warehouse: 740 Northwestern Avenue, Chicago, Illinois 60612

THIS TABLE RESERVED



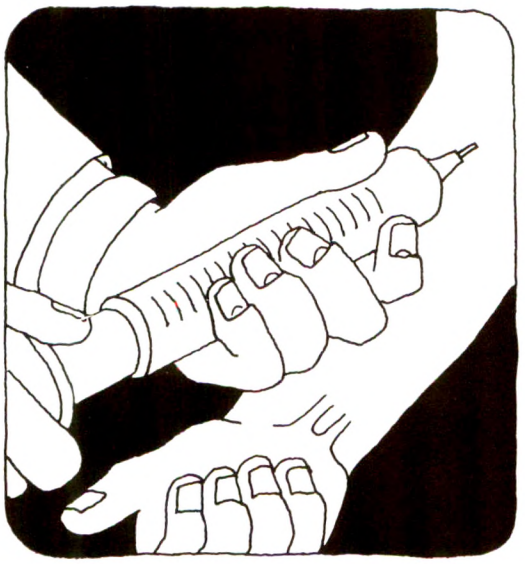
. . . yes, this Table is *reserved* for the hospital wanting the ultimate in modern urologic radiographic equipment. Powered for complete efficiency in cystoscopy and transurethral surgery and with built-in versatility to assure greatest diagnostic thoroughness in all of today's specialized radiographic procedures. Designed to accommodate image intensification units with associated cineradiographic or video tape equipment.

► ALSO RESERVED and waiting for you: New, colorful just-off-the-press literature illustrating and describing this outstanding Table. Write for your copy now—or ask your X-ray equipment supplier.

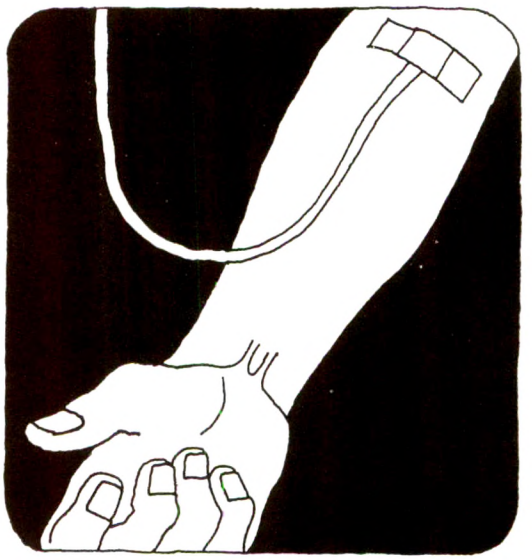
LIEBEL-FLARSHEIM®
SYBRON CORPORATION

CINCINNATI, OHIO 45215 • U.S.A.

Now...2 important I.V. Radiodiagnostic procedures for improved visualization



Adequate Dose Urography
with 50-60 ml. of 50% solution



Drip Infusion Pyelography
using between 250-400 ml. of a 25% solution*

Hypaque® 50%
sodium

brand of **sodium diatrizoate**

Winthrop

PIONEERS IN PRODUCTS FOR RADIOLOGIC DIAGNOSIS

*By diluting the 50% solution with an equal amount of sterile water for injection, USP, sodium chloride injection, USP, or dextrose injection, 5%, USP.

(Please see summary on following pages)

Hypaque® 50%
sodium
brand of **sodium diatrizoate**

Excretory Urography and Drip Infusion Pyelography

Description: Hypaque sodium is a sterile aqueous solution of sodium 3,5-diacetamido-2,4,6-triiodobenzoate, a radiopaque medium used to delineate internal structures.

Warning: Do not use Hypaque sodium for myelography. Injection of even a small amount into the subarachnoid space may produce convulsions and result in fatality.

General and Specific Precautions: Caution is advised in patients with a history of bronchial asthma, other allergic manifestations, or of sensitivity to iodine; these conditions represent a special risk, though not an absolute contraindication. To avoid or minimize possible allergic reactions, premedication with antihistamines may be considered. Benadryl (diphenhydramine hydrochloride) in the same syringe with Hypaque may result in precipitation. A test dose of contrast medium is not entirely reliable. Severe reactions, including fatalities, have occurred with a test dose as well as with the full diagnostic dose.

Caution is advised in patients with severe cardiovascular disease. In patients with impaired renal function and cardiovascular disease, drip infusion pyelography imposes a sudden osmotic and sodium load which can precipitate congestive heart failure. Contrast media injected into arteries or veins can promote sickling of red cells in susceptible individuals. In patients with reduced renal function, repeat of excretory or retrograde pyelography should be delayed at least 48 hours to avoid temporary suppression of urine. In preparation for excretory urography of patients with multiple myeloma, partial dehydration is not recommended, since this may predispose to the precipitation of myeloma protein in the kidney tubules. When thyroid function studies (PBI and 24-hour radioiodine uptake levels) are indicated, they should be performed *prior* to radiographic studies or several days afterwards, to avoid inaccurate results.

Hypaque sodium 50% should always be injected at body temperature.

General and Specific Adverse Reactions: Adverse reactions, usually of a minor nature, have occurred in 10-14 per cent of patients who have received Hypaque intravenously. Reactions due to *faulty technique* include hematomas and ecchymoses, following extravasation from the vein, and pyrogenic reactions. *Hemodynamic reactions* include vasodilatation with flushing, hypotension and, rarely, vein cramp or thrombophlebitis. Serious *cardiovascular reactions* include rare cases of cardiac arrhythmias (e.g., ventricular fibrillation), shock, and cardiac arrest. Transient proteinuria may occur occasionally following the injection of radiopaques and, rarely, oliguria and anuria have been reported secondary to a hypotensive reaction. *Allergic reactions* include asthmatic attacks, nasal and conjunctival symptoms, cutaneous reactions such as urticaria and, rarely, anaphylactic shock, sometimes with fatal outcome. Severe reactions may also be manifested by signs and symptoms relating to the *respiratory system* (dyspnea, cyanosis, pulmonary or laryngeal edema), or to the *nervous system* (restlessness, confusion, or convulsions). *Other reactions* include nausea, vomiting, excessive salivation, anxiety, headache, and dizziness. Infrequently, "iodism" (salivary gland swelling) from organic compounds appears two days after exposure and subsides by the sixth day. Reactions to drip infusion pyelography may not appear until some hours after the examination.

Angiography (Peripheral Arteriography and Venography)

Precautions *(See also General Precautions):* Extreme caution is advised in considering peripheral arteriography in patients suspected of having thromboangiitis obliterans (Buerger's disease). Any procedure (even needling or insertion of a catheter) may induce a severe arterial and/or venous spasm. Caution is also advisable in patients with severe ischemia associated with ascending infection.

Adverse Reactions *(See also General Adverse Reactions):* In addition to those listed under General Adverse Reactions, are those due to arterial trauma during the procedure (i.e., needling, insertion of catheter, subintimal injection, perforation, etc.) as well as to the hypertonicity or effect of the medium; also reported are transient arterial spasm, extravasation, hemorrhage, hematoma with tamponade, injury to nerves proximal to artery, thrombosis (rare in venography; if vein is irrigated following injection), dissecting aneurysm, arteriovenous fistula, (e.g., with accidental perforation of femoral artery and vein during needling) transient leg pain from contraction of calf muscles in femoral arteriography; transient hypotension after intraarterial (brachial) injection, and brachial plexus injury with axillary artery injections.

Cerebral Angiography: Because of the special techniques required, it is recommended that Hypaque sodium be used for this purpose only by persons skilled and experienced in carrying out this procedure.

Contraindication: Carotid angiography should be avoided during the progressive period of a stroke, since this increases the risk of cerebral complications.

Precautions *(See also General Precautions):* Select patients for this procedure with care. Use the 50 per cent solution with caution in extreme senility (but not old age, *per se*); advanced arteriosclerosis; severe hypertension; and cardiac decompensation.

The diagnostic value of the procedure, according to many authorities, when employed early enough in locating lesions amenable to surgery, may outweigh the added risk to patients who have recently experienced cerebral embolism or thrombosis (stroke syndrome). A small number of postangiographic fatalities, including progressive thrombosis, have occurred in which the procedure did not appear to play a role. Patients with severe cerebrovascular disease may be examined primarily by indirect methods of angiography.

Care should be exercised to avoid contaminating catheters, syringes, needles, and contrast media with glove powder or cotton fibers.

Angiography is hazardous in subarachnoid hemorrhage. In migraine, the procedure can be hazardous because of ischemic complications, particularly if performed during or soon after an attack.

Adverse Reactions *(See also General Adverse Reactions):* The major sources of complications are faulty technique, occlusive atherosclerotic vascular disease, repeated injections of the contrast media, and higher doses than those recommended.

Untoward reactions are mostly mild and transient, although permanent visual field defects and deaths have been reported.

(continued on next page)

(continued from preceding page)

Hypaque® 50%
sodium
brand of **sodium diatrizoate**

Vascular reactions: flushing, vessel spasm, thrombophlebitis, and cutaneous petechiae.

Neurologic complications: transient cerebral blindness, neuromuscular disorders, convulsions, coma, hemiparesis, unilateral dysesthesias, visual field defects, aphasia, and respiratory difficulties.

Aortography

Precautions *(See also General Precautions):* Special caution is advised to avoid inadvertent intrathecal injection when using the translumbar technique. The incidence and severity of reactions or complications that may occur are influenced by: the care and experience with which the procedure is performed; the amount and type of medium used; the age and condition of the patient; and the premedication and anesthesia used. Since aortography is not without some danger, it should be performed only by those experienced in the technique. Wherever possible, repeated injections of the solution during a single study should be avoided.

Adverse Reactions *(See also General Adverse Reactions):* Renal damage and shutdown; neurologic complications such as transverse myelitis or paraplegia; cardiovascular complications such as shock, cardiac arrest or failure, coronary occlusion, arterial thrombosis, embolism, and perforation of vessels; extravasation or hemorrhage from the puncture site or retroperitoneal catheter perforation; necrosis of the intestinal wall; acute pancreatitis; deaths; diffuse cutaneous petechiae; subintimal injection and aortic dissection.

Intraosseous Venography

See General Precautions and Adverse Reactions. A general anesthetic is sometimes necessary since the method is painful. Occasionally, extravasation of the contrast medium from the needle into the soft tissue may occur.

Direct Cholangiography

Precaution *(See also General Precautions):* This procedure should be used with caution in the presence of acute pancreatitis, injecting no more than 5 to 10 ml. without undue pressure.

Adverse Reactions *(See also General Adverse Reactions):* These may be attributed to injection pressure or excessive volume of the medium, resulting in overdistention. Such pressure may produce a sensation of epigastric fullness, followed by moderate pain in the back or right upper abdominal quadrant, which will subside when injection is stopped.

Some of the medium may enter the pancreatic duct and cause a transient serum amylase elevation 6 to 18 hours later, without apparent ill effects. Pancholangitis resulting in liver abscess has been reported. Occasionally, nausea, vomiting, fever, and tachycardia have been observed.

Hysterosalpingography

Contraindications: Menstruation, active or imminent; infection in any part of the genital tract, including the external genitalia; pregnancy, known or suspected. Use not advised for six months after end of pregnancy, or 30 days after conization or curettement.

Precaution *(See also General Precautions):* Caution should be exercised in patients with known or suspected carcinoma to avoid possible spread of the lesion by the procedure.

Splenoportography

Precautions *(See also General Precautions):* Procedure should be performed with caution on patients with blood dyscrasias, a tendency to severe bleeding, or a spleen recently become tender and palpable.

Adverse Reactions *(See also General Adverse Reactions):* Persistent hemorrhage with hemoperitoneum has been reported, and, in some instances, hemorrhage has required splenectomy.

How Supplied: Ampuls of 30 ml., boxes of 1, 10, and 25. A 1 ml. sensitivity test ampul is furnished with each ampul. Vials of 20 and 30 ml., rubber stoppered, boxes of 1, 10, and 25. Vials of 50 ml., rubber stoppered, boxes of 1 and 10. Each vial contains sufficient excess to permit withdrawal of 1 ml. for testing sensitivity.

If the solution is chilled, crystals may form but will readily dissolve if the ampul or vial is placed in moderately hot water before use. Cool to body temperature before injecting.

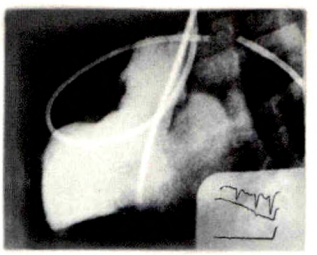
Winthrop

WINTHROP LABORATORIES, New York, New York 10016

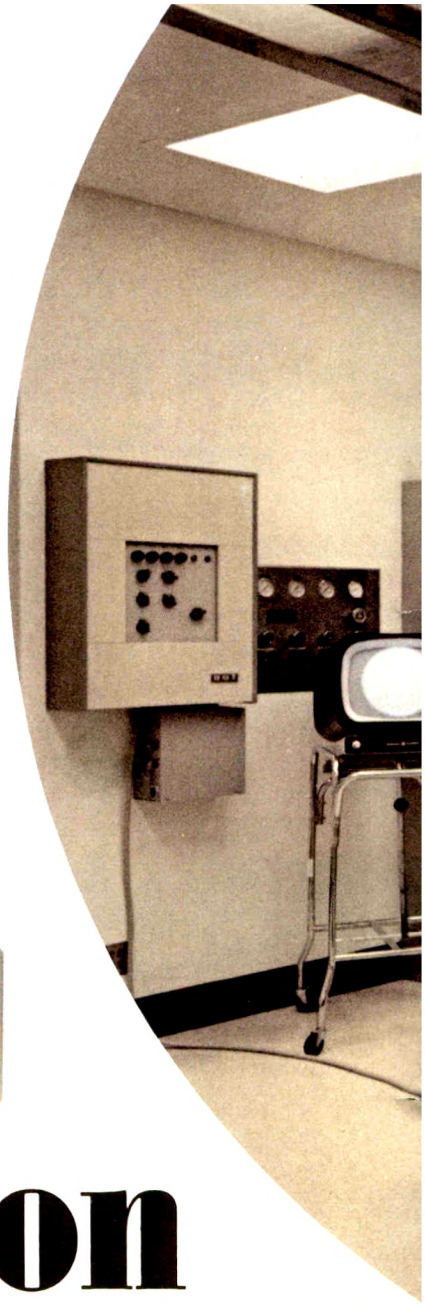
PIONEERS IN PRODUCTS FOR RADIOLOGIC DIAGNOSIS



data for decision...







total information

More precise, more readily available, than with any other medical system. And Fluoricon® II image intensification makes the difference.

Information. Getting all you need is your concern. Our responsibility. Information: Accurate. Easy to correlate. Sharp presentation. Anatomical and physiological information displayed as one image. Everything that's needed to make demanding diagnostic decisions. Complete in one package.

Only GE Fluoricon II image intensification, with exclusive CFPD (Cine Fluoro Physiological Display), delivers all this . . . provides the unmatched "information heartbeat" for vascular procedures systems. Dual field image intensification, with television presentation, allows maximum coverage in normal mode and peak resolution in magnified mode. Choose 16 or 35 mm cine, or phototimed 70 mm spot film camera with patient identification. Brightness is controlled automatically to present the sharpest image possible at all times.



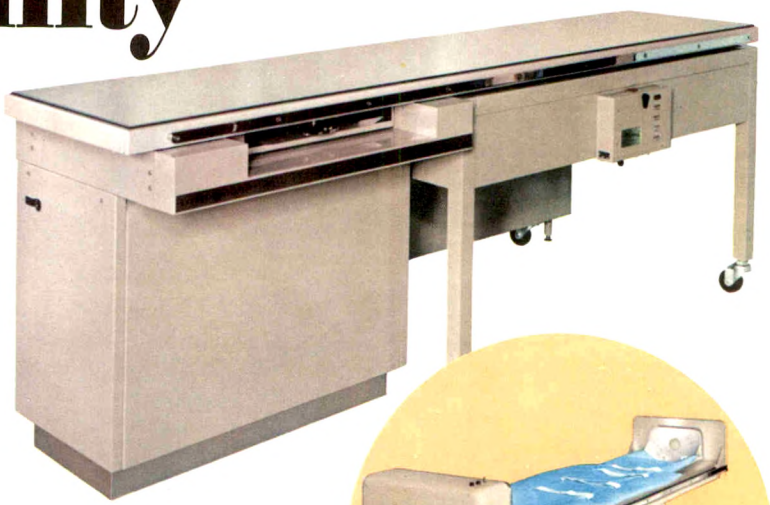
are recorded on cine film and displayed simultaneously on a TV monitor, and/or recorded on videotape. This filmed information is clear, accurate and precise. It presents your choice of from one to four channels of data — such as ECG, pressure(s), phonocardiograms and injection or other timed sequence sensitive data — in the combinations needed. CFPD facilitates the correlated cine study of both the physiological data and the actual anatomical image. Only GE offers this total information extra!

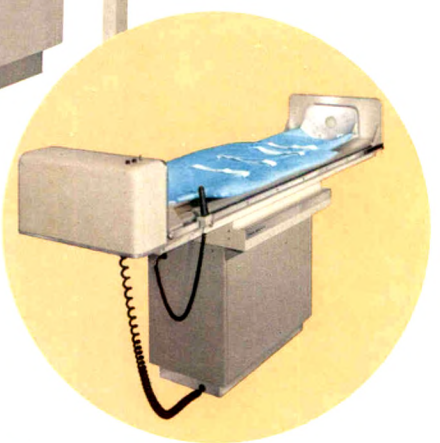
Whether it's for cardiovascular angiography, coronary arteriography, carotid/cerebral arteriography, abdominal arteriography, or cardiac catheterization and peripheral arteriography . . . GE Total Information Systems, with Fluoricon II image intensification, consistently deliver the critical information needed to make critical

GE MEDICAL SYSTEMS

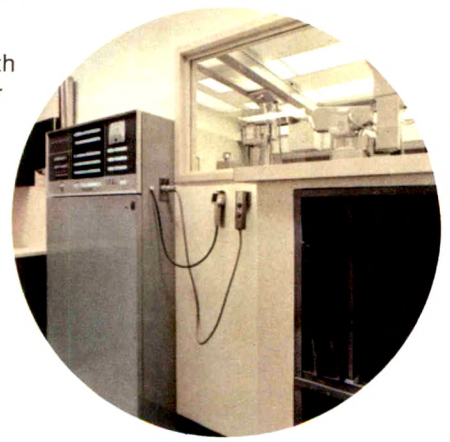


extended capability





New Model 75 catheterization table. Choice of tops: flat or rotating cradle. Top travels 55 inches longitudinally, permitting full use of rapid film changer and RIL seriograph; travels 10 inches laterally, 9 inches with Bucky. A push button on the control handle activates travel. Table height is adjustable at installation, 31-35 inches. A narrow 17 x 36 inch base allows doctor to work closer to patient without bending.



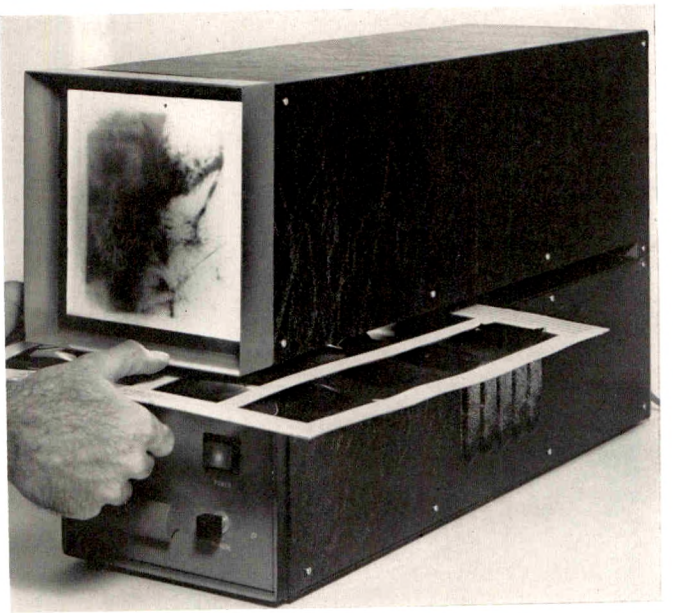
DXR-1250 3 phase, 12 pulse generator powers the system, with consistent linear output at all settings. Assures the power needed (i.e. 120 mAs in 1/10 of a second) for optimum contrast in rapid film changer applications.

Ask about Maxiservice®, the full-service leasing and maintenance plan that lets you get the equipment you need now, with payments you can afford out of normal operating funds. Includes periodic service by GE technicians. Result: You're always sure of a smooth-operating system . . . to keep the vital information coming continuously.

Progress is our most important product

GENERAL ELECTRIC

MILWAUKEE, WISCONSIN 53201



This system is described fully in the July 1968 issue of The American Journal of Roentgenology, p. 675-677. The viewer costs $495 F.O.B. Cambridge. Mounts are 55¢ depending on volume.

How Shintron's Accumat 70mm film system makes life easier on Radiologists. And Patients.

Shintron's Accumat System, developed at the Boston City Hospital, now enables you to store and view 70mm spot films with ease. The system consists of self-sealing film mounts and an automatic desk-top viewer. Sixteen spot films can be mounted in 15 seconds, identified and stored in the patient's film jacket. The viewing device enlarges image 3 times and with its wide angle screen permits viewing by several people at once for teaching seminars and conferences. In effect, with the Accumat System, you can now enjoy the advantages of 70mm spot films (such as reducing patient radiation dosage by as much as 90%) while eliminating the handling problems traditionally encountered with the 70mm technique. Write for full information today.

H. M. Anderson, Mgr., Medical Division
Shintron Co., Inc., 144 Rogers St.
Cambridge, Mass. 02142

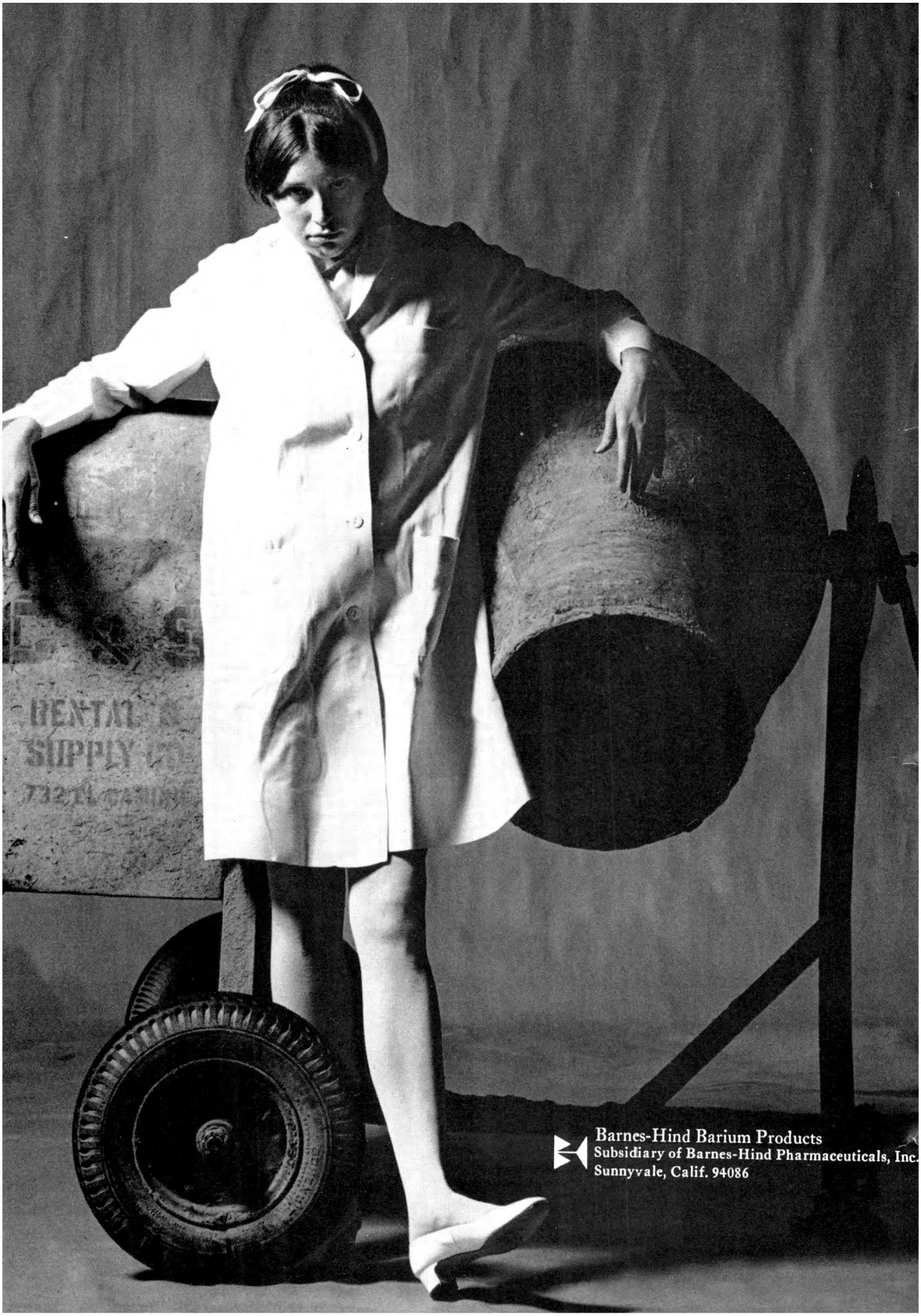
☐ I am interested in the Accumat System. Please send further information.
☐ Please send the name of the Accumat distributor in my area.

NAME _____

ADDRESS _____

CITY _____ STATE _____ ZIP _____

(Distributor inquiries are invited.)



Barnes-Hind Barium Products
Subsidiary of Barnes-Hind Pharmaceuticals, Inc.
Sunnyvale, Calif. 94086

The no-mix.

We took the construction work out of barium sulfate.

We premixed it into a smooth, creamy, instantly ready esophageal contrast medium.

Before, coating was often a hit-or-miss operation ('home-brewed' barium can be too thin, too thick or just plain settled out).

Not anymore.

Now, in seconds, you can photograph your patient's esophageal tract...easily take 3, 4, even 5, plates after an initial dose. In many patients the coating of Esophotrast lasts up to 15 minutes (ample time for fluoroscopy and radiography of the esophagus and evaluation of heart size).

Now you don't have to cajole your patients into drinking cupful after cupful of barium...the 1 oz. of Esophotrast, usually all that's needed, is nongritty and fruit-flavored–a really pleasant medium to take.

And it's just a squeeze of a tube away.

So why mix your own?

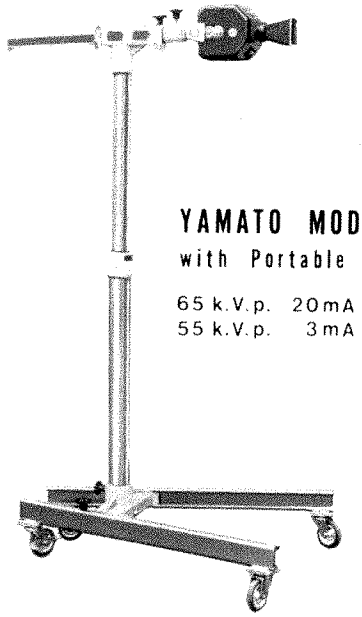
Esophotrast®

(barium sulfate)

Instantly ready esophageal cream

Recommended dose: 1 tablespoonful "chewed" thoroughly before swallowing. Repeat with a second tablespoonful to ensure prolonged adherence and coating of the esophageal mucosa.

PORTABLE X-RAY



YAMATO MODEL VII
with Portable Stand

65 k.V.p. 20mA 5 sec.
55 k.V.p. 3mA 2 min.

HIDA ELECTRIC APPARATUS INDUSTRIAL CO., LTD.
14-8, 2-chome, Yushima, Bunkyo-ku, Tokyo, Japan

HANLEY ECONOMY 14 x 17 X-RAY CABINET
SPECIAL DESIGN SLIDING DOORS
QUALITY AT LOW PRICES
Vertical Filing
We Build Special Size X-Ray Cabinets
SPECIAL SIZE, 33 H x 19½ D x 40 W, W/DOORS
5 COMPARTMENT SIZE—DIVIDERS 14 x 17 ..... $119.00
3 COMPARTMENT SIZE—DIVIDERS 14 x 17 ..... 90.00
APPROVAL GUARANTEED—F.O.B. FACTORY—CATALOGUE
HANLEY MEDICAL EQUIPMENT CO.
5614 South Grand X-ray Division St. Louis, Mo. 63111

THE NEW IMPROVED
STANFORD
X-RAY STEREOSCOPE
—CONSULTATION IN 3-D—



International usage for
over 30 years—be up to date
See Your X-Ray Dealer
—MADE IN USA—
SCHNEEMAN ELECTRONICS, INC.
GRANT'S PASS, OREGON

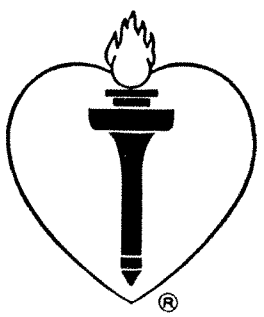
Your Heart Fund Fights

HEART ATTACK

STROKE

HIGH BLOOD PRESSURE

INBORN HEART DEFECTS



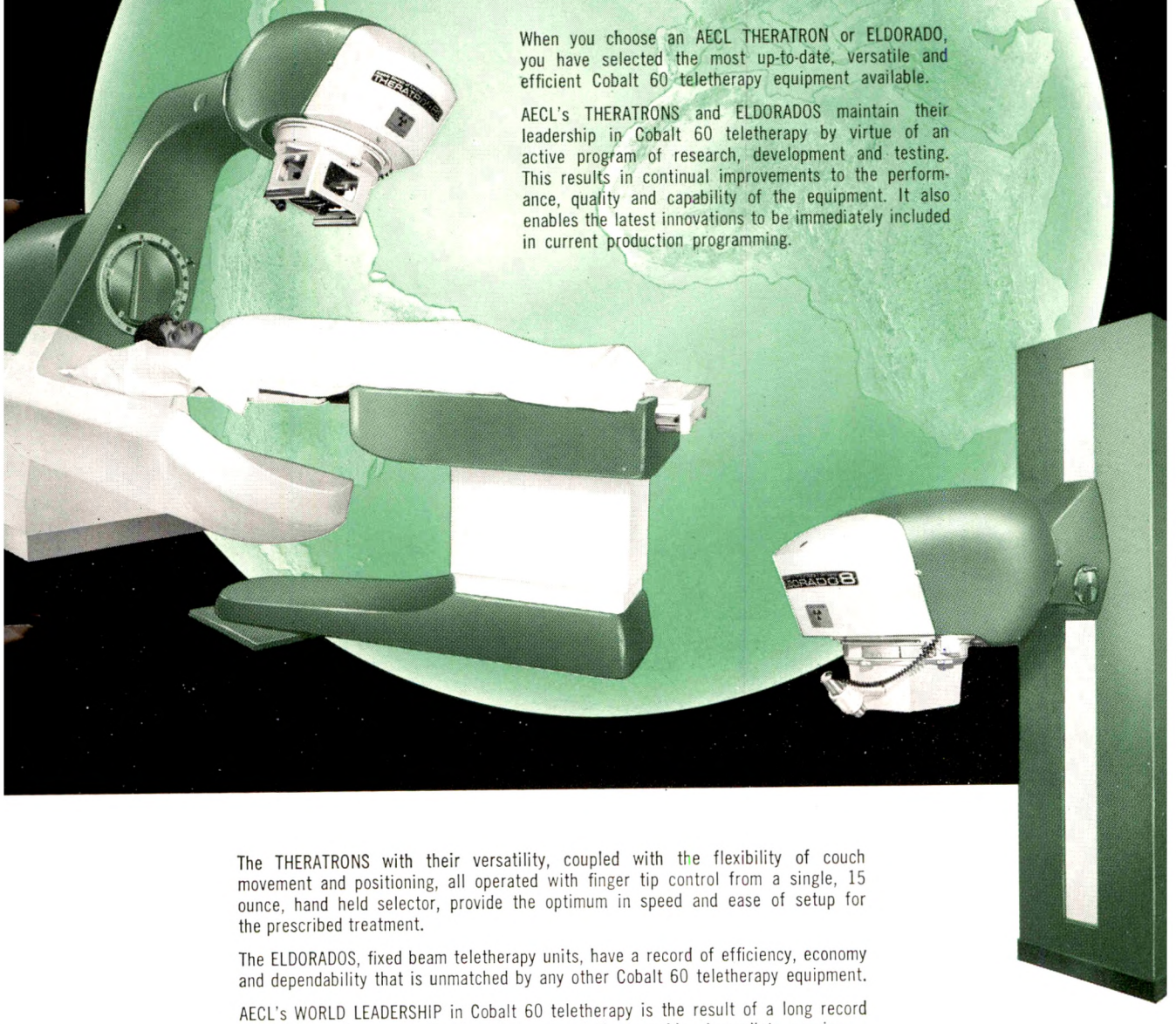
In reply to advertisers please mention that you saw their advertisement in
THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE
• • •
CHARLES C THOMAS
PUBLISHER
Springfield · Illinois

WORLD LEADERSHIP !

The choice of leading radiologists in 52 countries

When you choose an AECL THERATRON or ELDORADO, you have selected the most up-to-date, versatile and efficient Cobalt 60 teletherapy equipment available.

AECL's THERATRONS and ELDORADOS maintain their leadership in Cobalt 60 teletherapy by virtue of an active program of research, development and testing. This results in continual improvements to the performance, quality and capability of the equipment. It also enables the latest innovations to be immediately included in current production programming.



The THERATRONS with their versatility, coupled with the flexibility of couch movement and positioning, all operated with finger tip control from a single, 15 ounce, hand held selector, provide the optimum in speed and ease of setup for the prescribed treatment.

The ELDORADOS, fixed beam teletherapy units, have a record of efficiency, economy and dependability that is unmatched by any other Cobalt 60 teletherapy equipment.

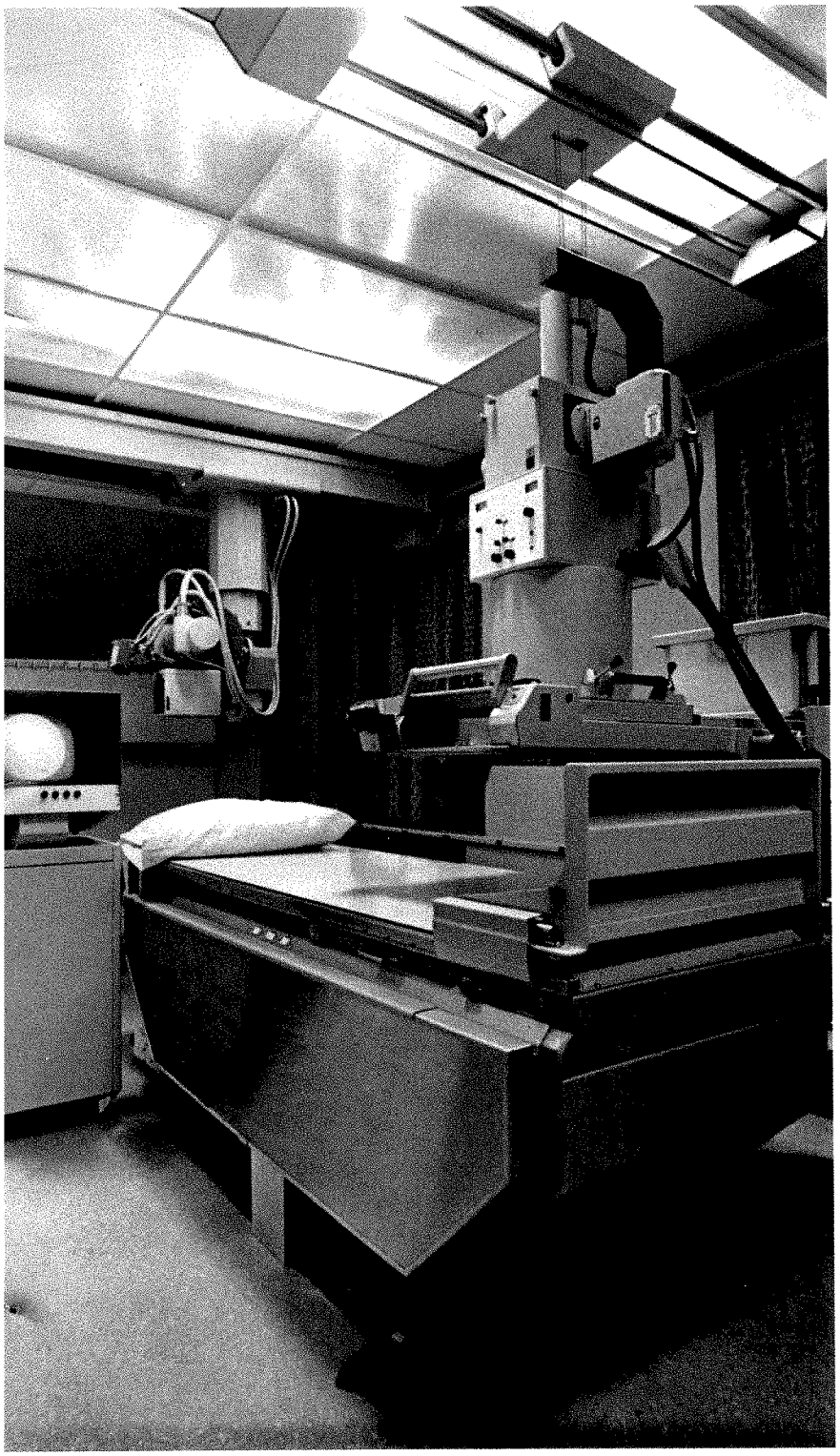
AECL's WORLD LEADERSHIP in Cobalt 60 teletherapy is the result of a long record of **proven performance.** World wide representation provides immediate service — anywhere! For detailed information please write to the address below.

Atomic Energy of Canada Limited
Commercial Products

68.3M

P.O. Box 93, Ottawa, Canada • Tel. 836-2790 • Area Code 613 • Cable 'NEMOTA'

One to grow on.



New Westinghouse imaging system can be modified easily-with interchangeable components to meet your future needs.

At left is the new Westinghouse IS-50 imaging system installed in a 300-bed community hospital. We call it CXR—Compatible X-Ray. Because every component in the system is compatible with all the others.

This means you can interchange, modify or add new components whenever your needs change. Take a look at this imaging system, with its optically equivalent three-port distributor.

Your present needs may call for a vidicon camera and a 16mm cine. But at any time you can add the exclusive Westinghouse 70mm rapid sequence spot film camera. Or 35mm cine—regular or high speed. Or an orthicon or plumbicon TV camera. Or image storage.

Every one fits. And any or all can be added anytime.

The same system-wide compatibility applies to tables, spot film devices, and generators. For example, solid state single phase and three phase controls can be upgraded to higher capacities for expanded requirements.

There's something else. When you buy a Westinghouse x-ray system, you never have to go it alone. Our sales and service organization has 500 people in 52 locations in the U.S. and Canada on call continually to meet your needs. Call your representative anytime. Westinghouse X-Ray Division, 2519 Wilkens Avenue, Baltimore, Maryland 21203.

J 03461

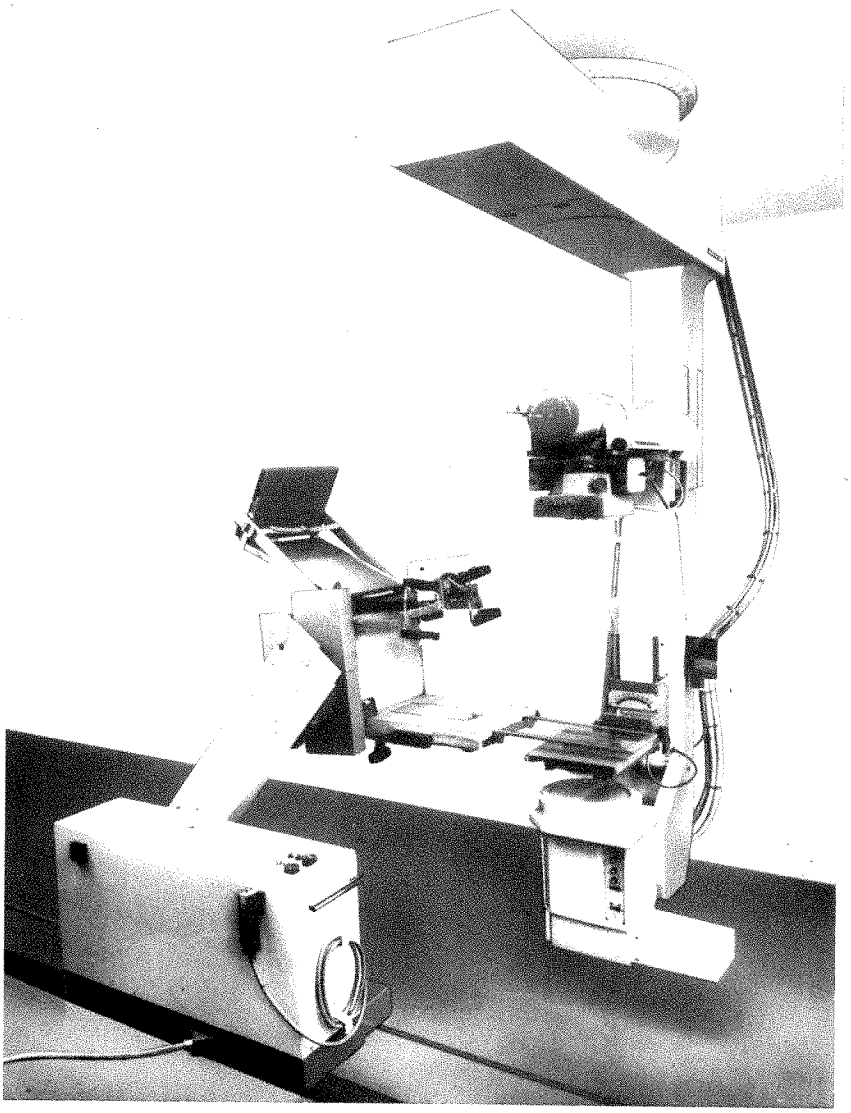
You can be sure . . . if it's

Westinghouse

MIMER III

NEURORADIOLOGICAL UNIT

WITH RCT-2 ROTATING CHAIR



Examinations:

Pneumo-encephalography
Ventriculography
Gas myelography
Cerebral angiography

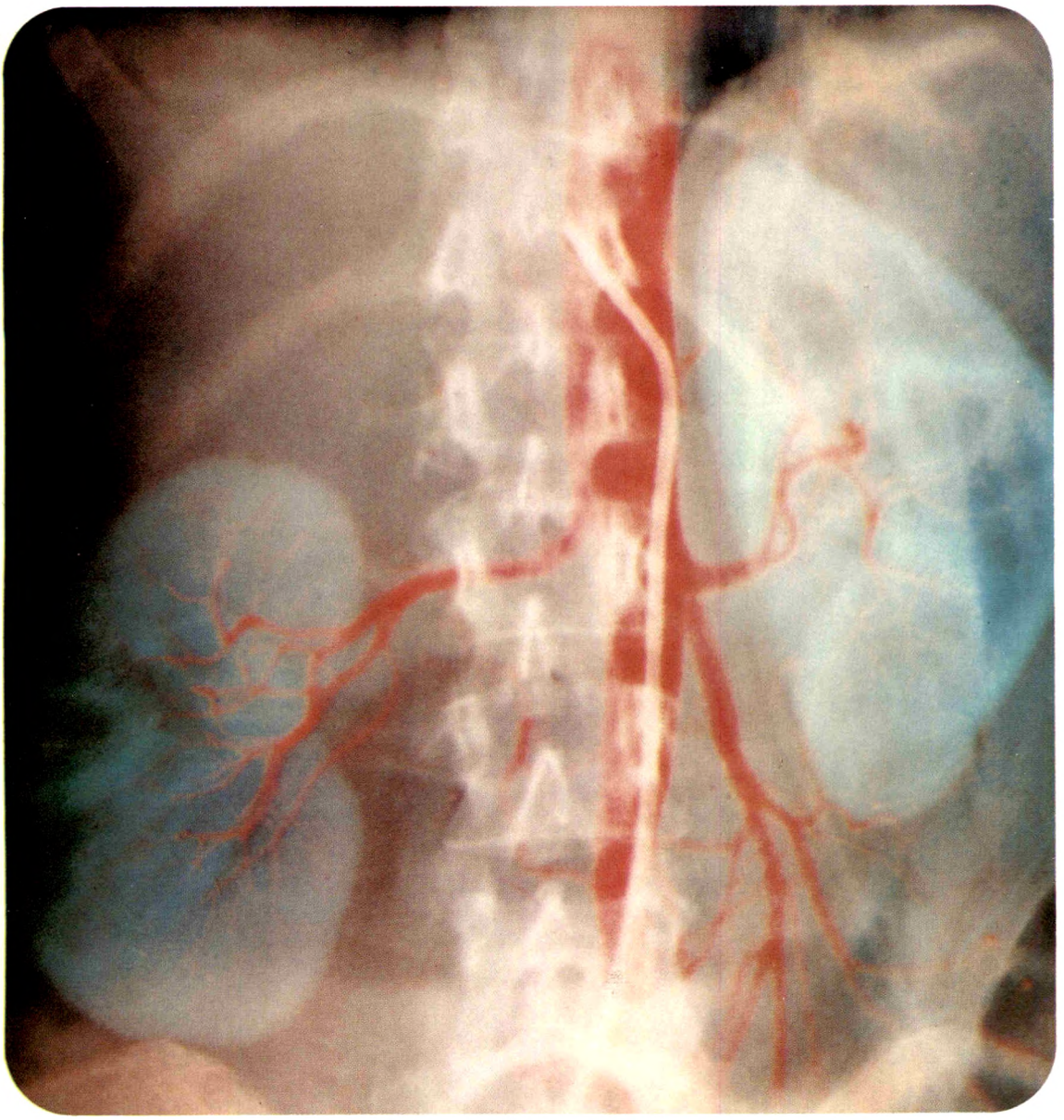
Techniques:

TV-Fluoroscopy
Laminography
Magnification
Standard radiography

ELEMA-SCHONANDER, INC., P.O. BOX 130, MT. PROSPECT, ILL. 60056
Tel. (312) 259-7206

Aortography

(percutaneous retrograde catheter technique) using Hypaque® sodium 50% as the contrast medium



The six color films illustrated, in which Hypaque was used as contrast medium, were supplied through the courtesy of Robert E. Wise, M.D. of the Lahey Clinic Foundation and New England Baptist Hospital, Boston, Mass. The technique, employing ordinary x-rays, is described in the Lahey Clinic Foundation Bulletin *14*:131, 1965.

and you'll get the same precise black-and-white definition using

Hypaque® 50%

sodium

brand of **sodium diatrizoate**

Aortography with Hypaque sodium 50% may give valuable evidence in cases of renal agenesis, duplications or ectopia, or of polycystic kidney. Aortograms are also of importance in helping to demonstrate aneurysmal change or the degree of patency of the arteriosclerotic vessel, and in aiding the surgeon to determine proper surgical management if such is needed especially where a stenotic vessel is responsible for life-threatening renal hypertension. Aortograms with Hypaque 50% have provided clearly defined needed evidence of pathology prior to surgical intervention.

Excretory Urography

using Hypaque® sodium 50% as the contrast medium*

*Color technique of Robert E. Wise, M.D.



and you'll get the same precise black-and-white definition using

Hypaque® 50%
sodium
brand of **sodium diatrizoate**

Excretory urography with Hypaque sodium 50% provides the detection of urinary tract lesions, without interference with functional activity, without age limit and without anesthesia—important advantages when instrumentation is undesirable.

Cerebral Arteriography

using Hypaque® sodium 50% as the contrast medium*

*Color technique of Robert E. Wise, M.D.



and you'll get the same precise black-and-white definition using

Hypaque® 50%

sodium

brand of **sodium diatrizoate**

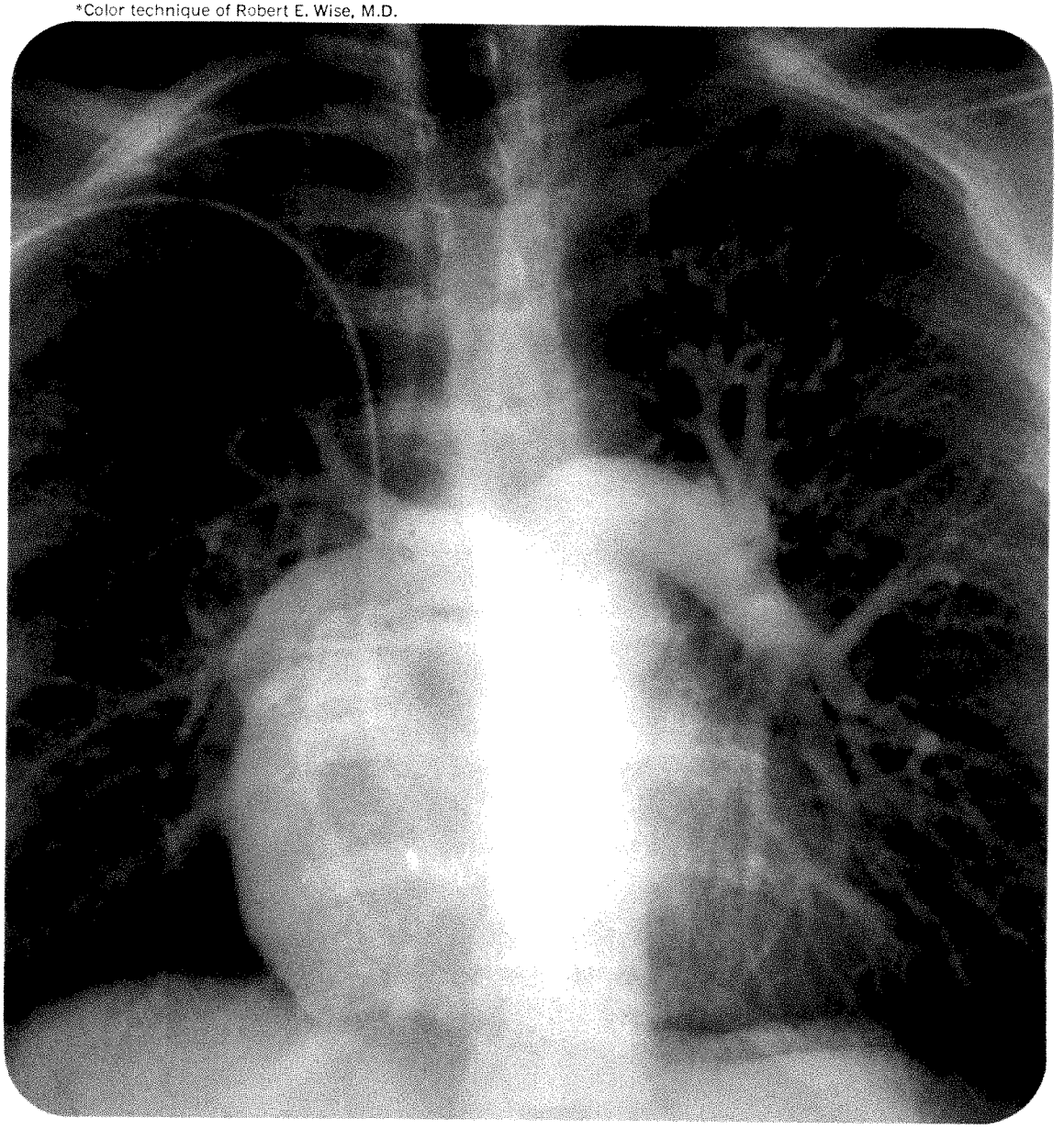
Cerebral arteriography with Hypaque sodium 50% has proved most useful in localizing and identifying intracranial lesions. Because it demonstrates both pathologic anatomy and physiology in such disorders as aneurysms, hematomas, angiomatous formations, meningiomas, glioblastoma multiforme, and other neoplasms, this procedure may provide diagnostic information frequently unobtainable by other means.

Please read the summary of prescribing information on the last pages of this unit.

Angiocardiography

using Hypaque®-M, 75% as the contrast medium*

*Color technique of Robert E. Wise, M.D.



and you'll get the same precise black-and-white definition using

Hypaque®-M, 75%

brand of **sodium and meglumine diatrizoates**

Because the cardiac chambers and great blood vessels of the thorax can be effectively visualized with Hypaque-M 75% (90% may be used alternatively), it provides an invaluable aid in the diagnosis of a variety of congenital and acquired cardiac defects. Angiocardiography has also proved useful in the study of neoplastic and infectious diseases of the heart. Hypaque-M 75% used for this purpose is freely miscible with blood, relatively non-irritating and nontoxic in recommended dosage, and is rapidly eliminated by the kidneys.

Nephrotomography

using Hypaque®-M, 90% as the contrast medium*

*Color technique of Robert E. Wise, M.D.



and you'll get the same precise black-and-white definition using

Hypaque®-M, 90%

brand of **sodium and meglumine diatrizoates**

One of the newer methods employed to reveal the nature of renal lesions is nephrotomography —a combination of rapid intravenous nephrography and body-section radiography which provides precise delineation of renal parenchyma. Nephrotomography with Hypaque-M 90% is used primarily to differentiate renal cysts from neoplasms, but may also be indicated to distinguish renal from extrarenal masses and to demonstrate congenital anomalies of the kidney.

Please read the summary of prescribing information on the last pages of this unit.

Retrograde Pyelography

using Hypaque® sodium 20% as the contrast medium*

*Color technique of Robert E. Wise, M.D.



and you'll get the same precise black-and-white definition using

Hypaque® 20%

sodium

brand of **sodium diatrizoate**

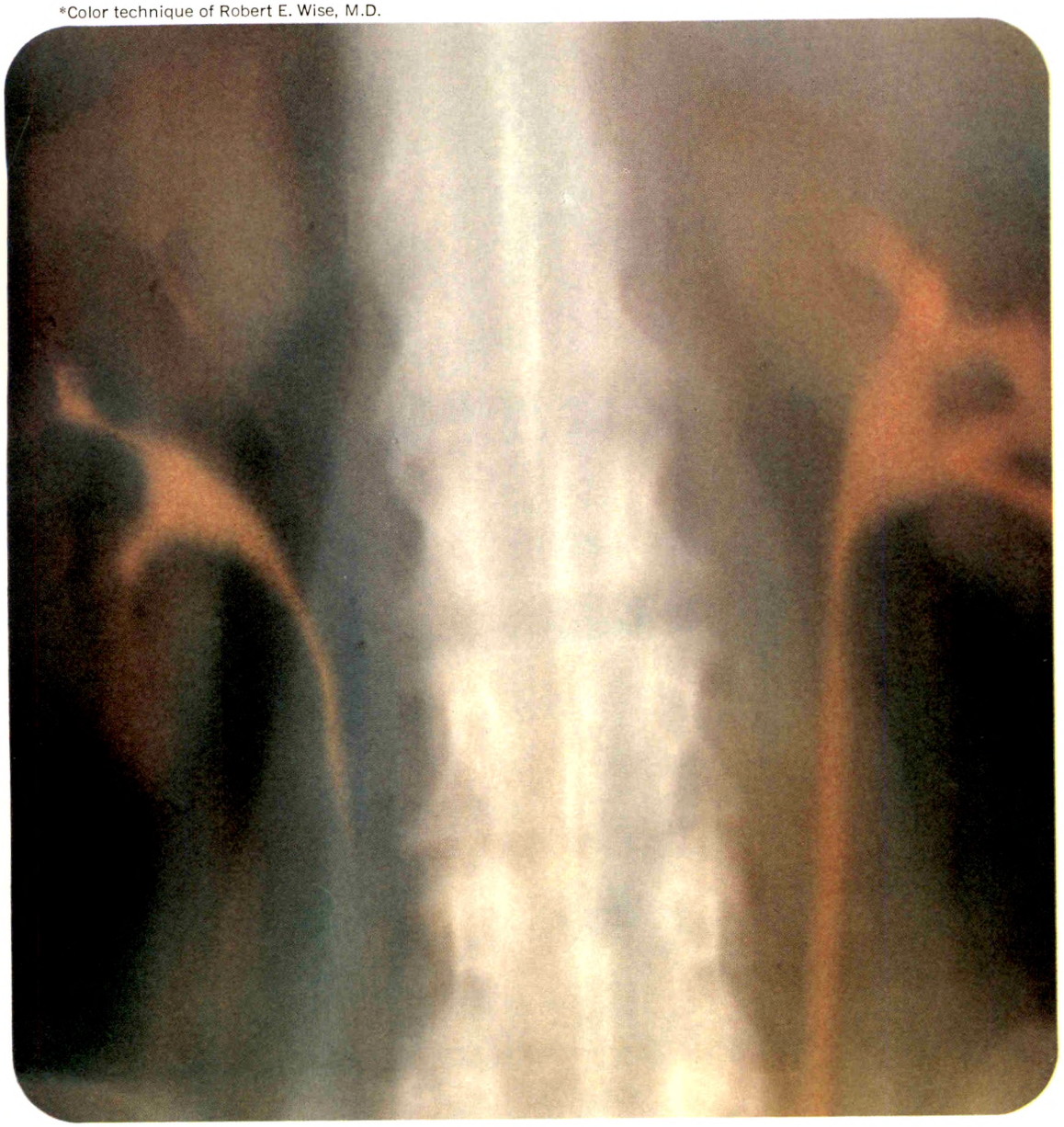
When loss of renal function or other causes result in unsatisfactory delineation of the urinary tract with intravenous techniques, retrograde pyelography with Hypaque sodium 20% solution can provide excellent anatomical details.

Please read the summary of prescribing information on the last pages of this unit.

Nephrotomography

using Hypaque®-M, 90% as the contrast medium*

*Color technique of Robert E. Wise, M.D.



and you'll get the same precise black-and-white definition using

Hypaque®-M, 90%

brand of **sodium and meglumine diatrizoates**

One of the newer methods employed to reveal the nature of renal lesions is nephrotomography —a combination of rapid intravenous nephrography and body-section radiography which provides precise delineation of renal parenchyma. Nephrotomography with Hypaque-M 90% is used primarily to differentiate renal cysts from neoplasms, but may also be indicated to distinguish renal from extrarenal masses and to demonstrate congenital anomalies of the kidney.

Please read the summary of prescribing information on the last pages of this unit.

Retrograde Pyelography

using Hypaque® sodium 20% as the contrast medium*

*Color technique of Robert E. Wise, M.D.



and you'll get the same precise black-and-white definition using

Hypaque® 20%

sodium

brand of **sodium diatrizoate**

When loss of renal function or other causes result in unsatisfactory delineation of the urinary tract with intravenous techniques, retrograde pyelography with Hypaque sodium 20% solution can provide excellent anatomical details.

Please read the summary of prescribing information on the last pages of this unit.

Unsurpassed
• CONTRAST
• TOLERANCE

Pathology precisely defined
with
Hypaque® sodium 50% and 20%
brand of **sodium diatrizoate**

50%, ampuls of 30 ml., vials of 20, 30 and 50 ml.
20%, bottles of 100 ml.

or with
Hypaque®-M, 75% and 90%
brand of **sodium and meglumine diatrizoates**

75%, vials of 20 and 50 ml.
90%, vials of 20 and 50 ml.

Summary of Full Prescribing Information

Hypaque® Sodium 50%
brand of **sodium diatrizoate, USP**

Sterile Aqueous Injection (Weight/Volume)

Excretory Urography and Drip Infusion Pyelography

Description: Hypaque sodium is sodium 3,5-diacetamido-2,4,6-triiodobenzoate, a radiopaque medium used to delineate internal structures.

Warning: Do not use Hypaque sodium for myelography. Injection of even a small amount into the subarachnoid space may produce convulsions and result in fatality.

General and Specific Precautions: Caution is advised in patients with a history of bronchial asthma, other allergic manifestations, or of sensitivity to iodine; these conditions represent a special risk, though not an absolute contraindication. To avoid or minimize possible allergic reactions, premedication with antihistamines may be considered. Benadryl (diphenhydramine hydrochloride) in the same syringe with Hypaque may result in precipitation. A test dose of contrast medium is not entirely reliable. Severe reactions, including fatalities, have occurred with a test dose as well as with the full diagnostic dose.

Caution is advised in patients with severe cardiovascular disease. In patients with impaired renal function and cardiovascular disease, drip infusion pyelography imposes a sudden osmotic and sodium load which can precipitate congestive heart failure. Contrast media injected into arteries or veins can promote sickling of red cells in susceptible individuals. In patients with reduced renal function, repeat of excretory or retrograde pyelography should be delayed at least 48 hours to avoid temporary suppression of urine. In preparation for excretory urography of patients with multiple myeloma, partial dehydration is not recommended, since this may predispose to the precipitation of myeloma protein in the kidney tubules. When thyroid function studies (PBI and 24-hour radioiodine uptake levels) are indicated, they should be performed *prior* to radiographic studies or several days afterwards, to avoid inaccurate results.

Hypaque sodium 50% should always be injected at body temperature.

General and Specific Adverse Reactions: Adverse reactions, usually of a minor nature, have occurred in 10-14 per cent of patients who have received Hypaque intravenously. Reactions due to *faulty technique* include hematomas and ecchymoses, following extravasation from the vein, and pyrogenic reactions. *Hemodynamic reactions* include vasodilatation with flushing, hypotension and, rarely, vein cramp or thrombophlebitis. Serious *cardiovascular reactions* include rare cases of cardiac arrhythmias (e.g., ventricular fibrillation), shock, and cardiac arrest. Transient proteinuria may occur occasionally following the injection of radiopaques and, rarely, oliguria and anuria have been reported secondary to a hypotensive reaction. *Allergic reactions* include asthmatic attacks, nasal and conjunctival symptoms, cutaneous reactions such as urticaria and, rarely, anaphylactic shock, sometimes with fatal outcome. Severe reactions may also be manifested by signs and symptoms relating to the *respiratory system* (dyspnea, cyanosis, pulmonary or laryngeal edema), or to the *nervous system* (restlessness, confusion, or convulsions). *Other reactions* include nausea, vomiting, excessive salivation, anxiety, headache, and dizziness. Infrequently, "iodism" (salivary gland swelling) from organic compounds appears two days after exposure and subsides by the sixth day. Reactions to drip infusion pyelography may not appear until some hours after the examination.

Angiography

(Peripheral Arteriography and Venography)

Precautions (See also General Precautions): Extreme caution is advised in considering peripheral arteriography in patients suspected of having thromboangiitis obliterans (Buerger's disease). Any procedure (even needling or insertion of a catheter) may induce a severe arterial and/or venous spasm. Caution is also advisable in patients with severe ischemia associated with ascending infection.

Adverse Reactions (See also General Adverse Reactions): In addition to those listed under General Adverse Reactions, are those due to arterial trauma during the procedure (i.e., needling, insertion of catheter, subintimal injection, perforation, etc.) as well as to the hypertonicity or effect of the medium; also reported are transient arterial spasm, extravasation, hemorrhage, hematoma with tamponade, injury to nerves proximal to artery, thrombosis (rare in venography; if vein is irrigated following injection), dissecting aneurysm, arteriovenous fistula, (e.g., with accidental perforation of femoral artery and vein during needling), transient leg pain from contraction of calf muscles in femoral arteriography; transient hypotension after intraarterial (brachial) injection, and brachial plexus injury with axillary artery injections.

Hypaque® Sodium 50% brand of **sodium diatrizoate (cont.)**

Cerebral Angiography: Because of the special techniques required, it is recommended that Hypaque sodium be used for this purpose only by persons skilled and experienced in carrying out this procedure.

Contraindication: Carotid angiography should be avoided during the progressive period of a stroke, since this increases the risk of cerebral complications.

Precautions (See also General Precautions): Select patients for this procedure with care. Use the 50 per cent solution with caution in extreme senility (but not old age, *per se*); advanced arteriosclerosis; severe hypertension; and cardiac decompensation.

The diagnostic value of the procedure, according to many authorities, when employed early enough in locating lesions amenable to surgery, may outweigh the added risk to patients who have recently experienced cerebral embolism or thrombosis (stroke syndrome). A small number of postangiographic fatalities, including progressive thrombosis, have occurred in which the procedure did not appear to play a role.

Patients with severe cerebrovascular disease may be examined primarily by indirect methods of angiography.

Care should be exercised to avoid contaminating catheters, syringes, needles, and contrast media with glove powder or cotton fibers.

Angiography is hazardous in subarachnoid hemorrhage. In migraine, the procedure can be hazardous because of ischemic complications, particularly if performed during or soon after an attack.

Adverse Reactions (See also General Adverse Reactions): The major sources of complications are faulty technique, occlusive atherosclerotic vascular disease, repeated injections of the contrast media, and higher doses than those recommended.

Untoward reactions are mostly mild and transient, although permanent visual field defects and deaths have been reported.

Vascular reactions: flushing, vessel spasm, thrombophlebitis, and cutaneous petechiae.

Neurologic complications: transient cerebral blindness, neuromuscular disorders, convulsions, coma, hemiparesis, unilateral dysesthesias, visual field defects, aphasia, and respiratory difficulties.

Aortography

Precautions (See also General Precautions): Special caution is advised to avoid inadvertent intrathecal injection when using the translumbar technique. The incidence and severity of reactions or complications that may occur are influenced by: the care and experience with which the procedure is performed; the amount and type of medium used; the age and condition of the patient; and the premedication and anesthesia used. Since aortography is not without some danger, it should be performed only by those experienced in the technique. Wherever possible, repeated injections of the solution during a single study should be avoided.

Adverse Reactions (See also General Adverse Reactions): Renal damage and shutdown; neurologic complications such as transverse myelitis or paraplegia; cardiovascular complications such as shock, cardiac arrest or failure, coronary occlusion, arterial thrombosis, embolism, and perforation of vessels; extravasation or hemorrhage from the puncture site or retroperitoneal catheter perforation; necrosis of the intestinal wall; acute pancreatitis; deaths; diffuse cutaneous petechiae; subintimal injection and aortic dissection.

Intraosseus Venography (See General Precautions and Adverse Reactions): A general anesthetic is sometimes necessary since the method is painful. Occasionally, extravasation of the contrast medium from the needle into the soft tissue may occur.

Direct Cholangiography

Precaution (See also General Precautions): This procedure should be used with caution in the presence of acute pancreatitis, injecting no more than 5 to 10 ml. without undue pressure.

Adverse Reactions (See also General Adverse Reactions): These may be attributed to injection pressure or excessive volume of the medium, resulting in overdistention. Such pressure may produce a sensation of epigastric fullness, followed by moderate pain in the back or right upper abdominal quadrant, which will subside when injection is stopped.

Some of the medium may enter the pancreatic duct and cause a transient serum amylase elevation 6 to 18 hours later, without apparent ill effects. Pancholangitis resulting in liver abscess has been reported. Occasionally, nausea, vomiting, fever, and tachycardia have been observed.

Hysterosalpingography

Contraindications: Menstruation, active or imminent; infection in any part of the genital tract, including the external genitalia; pregnancy, known or suspected. Use not advised for six months after end of pregnancy, or 30 days after conization or curettement.

Precaution (See also General Precautions): Caution should be exercised in patients with known or suspected carcinoma to avoid possible spread of the lesion by the procedure.

Splenoportography

Precautions (See also General Precautions): Procedure should be performed with caution on patients with blood dyscrasias, a tendency to severe bleeding, or a spleen recently become tender and palpable.
Adverse Reactions (See also General Adverse Reactions): Persistent hemorrhage with hemoperitoneum has been reported, and, in some instances, hemorrhage has required splenectomy.
How Supplied: Ampuls of 30 ml., boxes of 1, 10, and 25. A 1 ml. sensitivity test ampul is furnished with each ampul. Vials of 20 and 30 ml., rubber stoppered, boxes of 1, 10, and 25. Vials of 50 ml., rubber stoppered, boxes of 1 and 10. Each vial contains sufficient excess to permit withdrawal of 1 ml. for testing sensitivity.

If the solution is chilled, crystals may form but will readily dissolve if the ampul or vial is placed in moderately hot water before use. Cool to body temperature before injecting.

Hypaque® Sodium 20%

brand of **sodium diatrizoate**

Sterile Aqueous Solution 20% (weight/volume)

Precautions: It has long been known that oliguria or anuria may rarely follow bilateral retrograde pyelography or uncomplicated cystoscopic ureteral manipulation. Various mechanisms have been proposed to explain this occurrence, such as reflex anuria, edema, and occlusion of the ureteral orifices from local trauma, pressure, manipulation, sensitivity to the radiopaque medium or to residual disinfecting antiseptic on ureteral catheters, pyelotubular backflow, transient interstitial renal edema with increased pressure, and reduced renal blood flow. Because of the possibility of acute renal failure following bilateral retrograde pyelography, some authors conclude that retrograde pyelography should be done on only one side at a time.
Side Effects: The nonirritating properties of the medium minimize the likelihood of ureteropelvic spasm; in addition, a more natural outline of the upper urinary tract is obtained because of these properties. There is also a decrease in the incidence and severity of discomfort and colic following retrograde examination. Excellent tolerance was evidenced by notably few untoward reactions. Minor side reactions, which occurred in a few patients, consisted of nausea, vomiting, excessive salivation, and sweating. There was no indication of irritation of the urinary tract mucosa that could be attributed to the medium.

With Hypaque Sodium 20 per cent, reflux into the blood stream or lymphatics (pyelovenous or pyelolymphatic backflow) as a result of undue pressure of administration is not apt to result in a generalized reaction, since intravenous injection of more than double this concentration has been well tolerated.

Hypaque®-M, 75%

brand of **sodium and meglumine diatrizoates**

Sterile Aqueous Injection 75% (weight/volume)

Caution: The 75 per cent concentration is intended primarily for angiocardiography, nephrotomography and selected cases of peripheral angiography. Hypaque sodium (brand of diatrizoate sodium) 50 per cent solution is recommended for excretory urography, cerebral angiography and most cases of peripheral angiography.
Warning: Do not use Hypaque-M, 75 per cent for myelography. Injection of even a small amount into the subarachnoid space may produce convulsions and result in fatality.

Angiocardiography

Contraindications: Use of Hypaque-M, 75 per cent is contraindicated in patients with advanced renal destruction associated with severe uremia. Hypaque-M 75 per cent should not be used for myelography.
Precautions: 1. Caution is advised in patients with hyperthyroidism, hypertension, active tuberculosis and a history of allergy, especially to iodine. Angiocardiography and nephrotomography should be performed cautiously in patients with heart disease and circulatory failure and should not be employed in patients who are in collapse or who are critically ill or debilitated. A renal function test is advisable before administration of the 75 per cent solution.

2. Prior to the examination, the patient may be tested for sensitivity to the radiopaque medium. (See Side Effects and Sensitivity Tests.) Patients who show an idiosyncrasy should not be given the drug.

3. Premedication with a barbiturate is advisable if the patient is extremely nervous. Demerol (brand of meperidine), chlorpromazine and antihistamines have also been recommended for premedication. Such antihistamines as chlorpheniramine maleate or tripelennamine hydrochloride may be administered about 30 minutes before injection of the radiopaque medium or may be combined with it in a single injection. Many authorities recommend general anesthesia for small children and uncooperative patients.

4. Facilities for resuscitation including a mask with a breathing bag and pure oxygen should be available for immediate administration in case of severe reaction.

5. The sensations to be experienced should be described to the patient in order to allay apprehension before injection and to prevent excitement afterward.

6. To facilitate venipuncture, the needle should be sharp, the arm extended and the vein large and fully distended.

7. The syringe must be scrupulously clean in order to prevent sticking of the plunger during injection.

8. If crystals form, the solution should be warmed and agitated until they have redissolved. Injection should be made only when the solution is clear and is at a temperature of approximately 37.5° C.

9. Injection should be made only when there is free communication between needle and vein. When in doubt, another vein should be tried or the test postponed. Vein and needle should be watched during injection to prevent displacement of the needle or overdistention of the vein. If extravasation occurs, the injection should be stopped and a quantity of physiologic saline solution administered through the needle to dilute the radiopaque medium and to lessen the possibility of irritation.

10. Some authorities advise that repeated injections should not be given in close sequence and, if possible, should be avoided.

Side Effects and Sensitivity Tests: As with other radiopaque mediums, certain side effects occasionally may be encountered, although the 75 per cent solution has been well tolerated when given in recommended dosages. Serious complications following angiocardiography may be due to varying and perhaps unrelated factors. Symptoms may be due to the speed of injection and the anxiety and psychic stress associated with the examination, as well as to the material injected. Side effects will usually be minor and transient and may include a sensation of warmth and flushing, nausea, vein cramp, mild tachycardia, metallic or acid taste, tightness in the chest, headache, cough or urticaria. Delayed reactions may occur. Venous thrombosis has not been observed in patients receiving the 75 per cent solution, but as with any rapidly injected hypertonic solution, the possibility of this complication exists.

Angiocardiographic contrast mediums may produce symptoms of an anaphylactic nature in sensitive persons. Patients should be observed carefully during injection, as serious reactions including fatalities have occurred with most mediums. Since it is believed that reactions to intravenously administered organic iodine radiopaque agents are more likely to develop in patients with allergic diathesis, special care is advisable in persons with a history of asthma or other allergic manifestations.

Various methods have been advocated to detect sensitivity to contrast mediums, particularly conjunctival, oral, intradermal and intravenous testing. Conjunctival, oral and intradermal tests are not reliable, since reactions to them are generally caused by direct local vascular effect. Occasionally a severe reaction in the eye has followed a conjunctival test. An intravenous test is more likely to demonstrate sensitivity, although a negative reaction does not necessarily rule out the possibility. A small dose of 0.5 to 1 ml. is slowly injected intravenously over a period of one minute, followed by a period of observation sufficiently long to detect delayed reactions. Although allergic reactions generally occur quickly, occasionally they may not be manifested for 10 or even 15 minutes.

Warning signs and symptoms of possible intolerance or allergy include respiratory difficulty (wheezing, dyspnea or sensation of suffocation or tightness in the throat or chest), sneezing, itching, urticaria, nausea or vomiting and fainting.
Treatment of Reactions: (Same as with Hypaque Sodium 50%)

Nephrotomography

Contraindications, Precautions, Side Effects and Treatment of Reactions: See Angiocardiography.

Hypaque®-M, 90%

brand of **sodium and meglumine diatrizoates**

Sterile Aqueous Injection 90% (weight/volume)

Caution: Hypaque-M, 90 per cent is intended primarily for angiocardiography, nephrotomography, hysterosalpingography and selected cases of peripheral angiography. Hypaque sodium

Hypaque®-M, 90%
brand of **sodium and meglumine diatrizoates (cont.)**

50 per cent solution is recommended for excretory urography, cerebral angiography and most cases of peripheral angiography.
Warning: Do not use Hypaque-M, 90 per cent for myelography. Injection of even a small amount into the subarachnoid space may produce convulsions and result in fatality.

Angiocardiography

Contraindications: Use of Hypaque-M, 90 per cent is contraindicated in patients with advanced renal destruction associated with severe uremia. Hypaque-M, 90 per cent should not be used for myelography.
Precautions: 1. Caution is advised in patients with hyperthyroidism, hypertension, active tuberculosis and a history of allergy, especially to iodine. Angiocardiography and nephrotomography should be performed cautiously in patients with heart disease and circulatory failure and should not be employed in patients who are in collapse or who are critically ill or debilitated. A renal function test is advisable before administration of Hypaque-M, 90 per cent.

2. Prior to the examination, the patient may be tested for sensitivity to Hypaque-M, 90 per cent. (See Side Effects and Sensitivity Tests.) Patients who show an idiosyncrasy to Hypaque-M, 90 per cent should not be given the drug.

3. Premedication with a barbiturate is advisable if the patient is extremely nervous. Demerol (brand of meperidine), chlorpromazine and antihistamines have also been recommended for premedication. Such antihistamines as chlorpheniramine maleate or tripelennamine hydrochloride may be administered about thirty minutes before injection of Hypaque-M, 90 per cent or may be combined with it in a single injection. Many authorities recommend general anesthesia for small children and uncooperative patients.

4. Facilities for resuscitation including a mask with a breathing bag and pure oxygen should be available for immediate administration in case of severe reaction.

5. The sensations to be experienced should be described to the patient in order to allay apprehension before injection and to prevent excitement afterward.

6. To facilitate venipuncture, the needle should be sharp, the arm extended and the vein large and fully distended.

7. The syringe must be scrupulously clean in order to prevent sticking of the plunger during injection.

8. Hypaque-M, 90 per cent should be warmed and agitated until all suspended crystals have redissolved. Injection should be made only when the solution is clear and is at a temperature of approximately 37.5°C.

9. Injection should be made only when there is free communication between needle and vein. When in doubt, another vein should be tried or the test postponed. Vein and needle should be watched during injection to prevent displacement of the needle or overdistention of the vein. If extravasation occurs, the injection should be stopped and a quantity of physiologic saline solution administered through the needle to dilute the Hypaque-M, 90 per cent and to lessen the possibility of irritation.

10. Some authorities advise that repeated injections should not be given in close sequence and, if possible, should be avoided.

Hypaque®-M, 90%
brand of **sodium and meglumine diatrizoates (cont.)**

Side Effects and Sensitivity Tests: Serious complications following angiocardiography may be due to varying and perhaps unrelated factors. Symptoms may be due to the speed of injection and the anxiety and psychic stress associated with the examination, as well as to the material injected. Side effects noted with Hypaque-M, 90 per cent were usually of a minor and transient nature and included a sensation of flushing or warmth, nausea, vein cramp, mild tachycardia, metallic or acid taste, tightness in the chest, headache, cough or urticaria. Delayed reactions may occur. Venous thrombosis has been observed in patients following the percutaneous insertion of the injection needle. This complication may be anticipated, however, when concentrated hypertonic solutions are injected rapidly. In skilled hands, the administration of Hypaque-M, 90 per cent is attended by comparatively few untoward reactions.

Angiocardiographic contrast mediums may produce symptoms of an anaphylactic nature in sensitive persons. Patients should be observed carefully during injection, as serious reactions including fatalities have occurred with most mediums. Since it is believed that reactions to intravenously administered organic iodine radiopaque agents are more likely to develop in patients with allergic diathesis, special care is advisable in persons with a history of asthma or other allergic manifestations.

Various methods have been advocated to detect sensitivity to contrast mediums, particularly conjunctival, oral, intradermal and intravenous testing. Conjunctival, oral and intradermal tests are not reliable, since reactions to them are generally caused by a direct local vascular effect. Occasionally a severe reaction in the eye has followed a conjunctival test. An intravenous test is more likely to demonstrate sensitivity, although a negative reaction does not necessarily rule out the possibility. A small dose of from 0.5 to 1 ml. is slowly injected intravenously over a period of one minute, followed by a period of observation sufficiently long to detect delayed reactions. Although allergic reactions generally occur quickly, occasionally they may not be manifested for ten or even fifteen minutes.

Warning signs and symptoms of possible intolerance or allergy include respiratory difficulty (wheezing, dyspnea or sensation of suffocation or tightness in the throat or chest), sneezing, itching, urticaria, nausea or vomiting and fainting.
Treatment of Reactions: (Same as with Hypaque Sodium 50%)

Nephrotomography

Contraindications, Precautions, Side Effects and Treatment of Reactions: See Angiocardiography.

Hysterosalpingography

Contraindications: The procedure should not be performed during the menstrual period or when menstrual flow is imminent, nor should it be performed when infection is present in any portion of the genital tract, including the external genitalia. The procedure is also contraindicated for pregnant women or for those in whom pregnancy is suspected. Its use is not advised for six months after termination of pregnancy, or for thirty days after conization or curettement.
Precautions: In patients with carcinoma or in those in whom the condition is suspected, caution should be exercised to avoid possible spread of the lesion by the procedure.

Pathology Precisely Defined

Hypaque® Sodium 20% and 50%
brand of **sodium diatrizoate**

Hypaque®-M, 75% and 90%
brand of **sodium and meglumine diatrizoates**

Winthrop **PIONEERS IN PRODUCTS FOR RADIOLOGIC DIAGNOSIS**

PRINTED IN U.S.A. ISSUED JAN. 1969 (1326M)

THE AMERICAN JOURNAL OF ROENTGENOLOGY
RADIUM THERAPY AND NUCLEAR MEDICINE

VOL. 105 FEBRUARY, 1969 NO. 2

THE LUNG: THE CHALLENGE OF NUCLEAR MEDICINE*

By JAMES LELAND QUINN, III†
CHICAGO, ILLINOIS

The name of Hampton in radiology is one which first became known to me when I was a freshman medical student in 1955, the year Dr. Hampton's medical career ended.

His name kept coming up time and time again through my medical student and resident years as his contributions became more and more a part of my radiology reading.

The HAMPTON TECHNIQUE *for examining patients with acute upper gastrointestinal tract hemorrhage; the* HAMPTON MANEUVER *to obtain diagnostic air contrast roentgenograms of the antrum and proximal duodenum in patients with peptic ulcer disease; the* HAMPTON HUMP, *a pleural based convex density toward the hilum in pulmonary infarctions; and the* HAMPTON LINE, *mucosal edema contrasted against a barium filled benign gastric ulceration, are a few of his contributions to Radiology.*

Dr. Hampton made many other contributions to our radiologic knowledge through his classic descriptions of lipoid pneumonia,[5] middle lobe pathology[6] and intervertebral disk disease.[7] For me, his most outstanding contribution was his collaborative work with Dr. Benjamin Castleman on the correlation of chest roentgenograms with necropsy findings.[8] This is a classic paper and should be read by every physician interested in pulmonary embolus and infarct.

Dr. Dabney Kerr, commenting on the paper, in many ways summarized a recurring theme in Dr. Hampton's publications when he said, "There has been very little theorizing in the presentation of this excellent work, and we have been given a maximum of factual evidence, which, it seems to me, is one of the things which we as roentgenologists need most."

Aubrey Hampton, or "Hamp" as his friends called him, was born in Capeville, Texas, in 1900. He received his medical degree at Baylor University in 1925. After an internship and a period as City Physician in Fort Worth, he began his radiology training under Dr. George Holmes at the Massachusetts General Hospital. He remained as a staff radiologist and when Dr. Holmes retired in 1941, was appointed Radiologist-in-Chief.

* First Memorial Lecture to Aubrey Otis Hampton, 1900–1955. Presented at the Massachusetts General Hospital, Boston, Massachusetts, April 24, 1968.

† Professor of Radiology, Northwestern University, Chicago, Illinois.

During World War II, Dr. Hampton became head of the Radiologic Services at Walter Reed Army Hospital. He remained in Washington after the war as Chief of Radiology at Garfield Memorial Hospital. While in Washington he also served as consultant to the National Institutes of Health and the Veterans Administration, became a member of the National Research Council, and was a major force in the establishment of the Radiologic Pathology Registry at the Armed Forces Institute of Pathology.

In December, 1953, Dr. Hampton suffered a coronary occlusion. He returned to his work in February, 1954, but increasing cardiac problems caused him to retire in May, 1955. On July 17, at his summer home in South Weare, New Hampshire, he suffered a fatal stroke.

His contributions to his chosen field were truly outstanding. Former residents of his that I have talked with had the greatest respect for his objectivity, mental prodding and complete charm.

YOU may ask why I chose the title, "The Lung: The Challenge of Nuclear Medicine" for this Lecture, and what it has to do with Dr. Hampton!

I chose the lung because of the great interest and the contributions to understanding pulmonary disease with which Dr. Hampton was associated. I choose to call it a challenge because we who are involved in radionuclide lung scanning have serious problems which need solutions and important questions which need answers.

We all can learn a great deal from the approach to medical problems, the unswerving objectivity and the ability to separate the wheat from the chaff which characterized Dr. Hampton's professional career.

There is always a certain anxiety among the established community when an advance occurs. This is partly due to the anti-environmental nature and challenge of the advance. As small advances add up, anxiety increases. This anxiety is not as evident among younger students, since they accept this readily as a part of the "new" diagnostic environment, having modes of sensory perception we may have lost long ago.

Anxiety is further enhanced when the establishment attempts to solve the problems of today with the tools of the past. This again is more prevalent among the older, and perhaps polarized, medical community than the younger men.

We, the established, always refer to our students as being our best teachers because they inspire us through their continual prodding and assault on vulnerable "truths." In fact, what they are doing is educating us to assimilate the new environment in a world where the flexible survive and the polarized wilt.

When there are absent or strained lines of communication between the established and the developing generations, there is conflict and rebellion. This is very much in evidence today in fields outside of medicine. It is remarkably absent in medicine or in radiology because of our "teach-in" concepts, which switch the educational process from package to discovery. The bedside rounds or x-ray conferences encourage debate and expose deficiencies in diagnosis and become a scene where the audience does an enormous amount of work.

One of our major problems is in communication between established medical specialists. This gap widens and anxiety is further heightened by the literature reports which I refer to as *competitive communication*, and is exemplified by angiographers saying their procedure is better than lung scanning and scanners countering with claims promoting their vested interests.

It is this communication gap between Nuclear Medicine and her sister radiologic disciplines which is one of the major challenges to Nuclear Medicine today.

NUCLEAR MEDICINE

Nuclear Medicine is the clinical discipline which has grown out of the many diagnostic, therapeutic and investigative applications of radionuclide techniques. As an ancillary diagnostic procedure, radio-

nuclide methodology may provide new, early, more reliable or more specific information concerning normal or abnormal body structure or function.

In many ways the growth and development of lung scanning exemplifies the application of radioactive substances in the diagnosis and management of disease states.

Lung scanning grew out of a need to improve the diagnosis of pulmonary embolism and infarct. Since Virchow's classic description of the predisposing conditions which lead to venous thrombosis, the medical literature has been filled with articles pointing out the difficulty in diagnosing pulmonary embolism. In this regard, problem finding was simple. Problem solving using a scan technique was another matter.

LUNG SCAN DEVELOPMENT

In the summer of 1962, Dr. Edward Carr and his associates at the University of Michigan reported on a scanning technique which permitted them to diagnose experimental myocardial infarct in dogs using radiochlormerodrin.[1] This prompted our group to try to apply the technique in pulmonary infarction.

A model for pulmonary embolus was developed. It involved the simple introduction of a sponge into the exposed jugular vein of a dog and the directing of it into the right atrium with a plunger. Except for a few instances when the sponge was pushed into the axillary vein, the infarction process, described by Hampton and Castleman in their excellent article, was obtained. To quote from their article,[8] "During the first day and probably the second day of infarction, there is no definite destruction of alveolar walls. There is merely a very marked congestion of the capillaries and diapedesis of the red blood cells into the dilated alveoli of the region involved. After the second day there is beginning necrosis of the alveolar walls and degeneration of the red blood cells."

Using this model we investigated available radiopharmaceuticals. The best we found was chlormerodrin which gave a 2:1 ratio of normal to an infarcted lung. This difference could only be detected by scanning the lungs in a collapsed state outside of the thoracic cage.

At the 1963 Society of Nuclear Medicine meeting we reported that this pulmonary embolus model would be satisfactory in evaluating newer lung scanning radiopharmaceuticals.[11,12] At that meeting Dr. George Taplin and his associates[20] of UCLA described the aggregation of iodinated human serum albumin into particle sizes large enough to be trapped temporarily by the pulmonary capillary bed.

Upon returning to North Carolina, we applied the Taplin albumin macroaggregates to our embolus model and obtained excellent results.[22]

Our first lung scans in patients, as did those by the parallel development work at Johns Hopkins of Wagner and MacAfee, quickly brought us to the realization that we had a very sensitive depictor of pulmonary blood flow, and that a cautious approach to the diagnosis of pulmonary embolus was in order.[13,14]

DETECTORS AND AGENTS

The most common instrument used to image the distribution of the radioactive macroaggregate is the rectilinear scanner with one or two moving detector crystals with focused collimators.

An important advance in nuclear medical instrumentation occurred when a stationary device, developed by Mr. Hal Anger at Berkeley, became available commercially. This machine has a large detector crystal with parallel rather than focused collimation and has a field of view 9 to 12 inches in diameter. One of the sad commentaries on our young field is that these two types of instruments, camera and scanner, are frequently placed in competition, one with the other. These two instruments have different depth responses and should be thought of as having advantages one over the other in certain imaging situations.

Several radionuclide tags for the macroaggregated albumin (RAMA) have been used, the most common being iodine 131

and technetium 99m. The dose of I^{131} in perfusion scanning is 100–300 μc and for Tc^{99m}, 500–3,000 μc.

A newer radionuclide being evaluated for perfusion scanning is indium 113m.[19] This radioisotope has a 390 kev. gamma-ray emission and a physical half-life of 1.7 hours. Because of the short half-life and almost pure gamma emission, multimillicurie amounts of In^{113m} and Tc^{99m} can be given without undue patient radiation exposure.

CAUSES OF NONUNIFORM PERFUSION

Soon after we began scanning lungs our ignorance of the myriad of nonembolic causes of altered pulmonary perfusion became known to us, mainly through our missed diagnoses (Table 1). With our animal experiments we discovered that occlusion of the diaphragmatic artery, of the diaphragmatic vein, or the creation of a lobar hypoxia with intrabronchial nitrogen, all give the same lung picture, absent perfusion in the area involved (Fig. 1). Overinflation of the lung decreased perfusion to that area, but to a lesser degree than the literature would suggest.[10]

Gravity alone will cause nonuniform pulmonary perfusion. In the erect or decubitus position, the dependent lung is more richly perfused.

Thrombi or emboli of any cause will result in nonuniform pulmonary perfusion. Pulmonary artery wall disease also will be associated with alterations in pulmonary perfusion.

PULMONARY EMBOLUS

The major application of lung scanning in medicine today is still the early diagnosis of pulmonary embolus. It is a safe and simple procedure and should be performed as soon as possible in patients where there is the slightest suspicion that pulmonary emboli may exist.

Pulmonary embolus remains the leading cause of unexpected death among hospitalized patients. Recent reports have emphasized its occurrence in as many as 20 per cent of postcardiac surgery patients,[3] 6 per cent of orthopedic patients,[21] and 3 per cent of psychiatric patients confined to their beds.[9]

Pulmonary embolic disease may be a major etiologic factor in acquired pulmonary hypertension.[4]

TABLE I

CAUSES OF NONUNIFORM PULMONARY PERFUSION

(As Depicted by Lung Scans)

1. Gravity or Acceleration
   - Vertical and lateral
   - Not forward or reverse

2. Thrombi or Emboli
   - (a) Blood clot
   - (b) Tumor
   - (c) Fat
   - (d) Oil (lymphangiogram)
   - (e) Air
   - (f) Parasites

3. Pulmonary Artery Wall Disease
   - (a) Arteritis (tuberculosis)
   - (b) Hypoplasia

4. Pulmonary Artery or Vein Compression by
   - (a) Mediastinal masses
   - (b) Tension (pneumothorax)
   - (c) Fluid (hydrothorax > 1,500 cc.)

5. Pulmonary Venous Hypertension
   (Mitral valvular disease)

6. Alveolar Hypoxia
   - (a) Bronchial tumors
   - (b) Mucus plugs
   - (c) Blood
   - (d) Pneumonia
   - (e) Asthma

7. Vascular Bed Destructionor Compression
   - (a) Emphysema
   - (b) Abscess
   - (c) Pneumonia
   - (d) Loculated effusion
   - (e) Neoplasm

8. Shunts
   - (a) Congenital, *e.g.*, patent ductus arteriosus, hemangioma, sequestration
   - (b) Acquired, *e.g.*, surgery, emphysema

9. Increased Alveolar Pressure
   - (a) Asthma
   - (b) Ball-valve obstruction

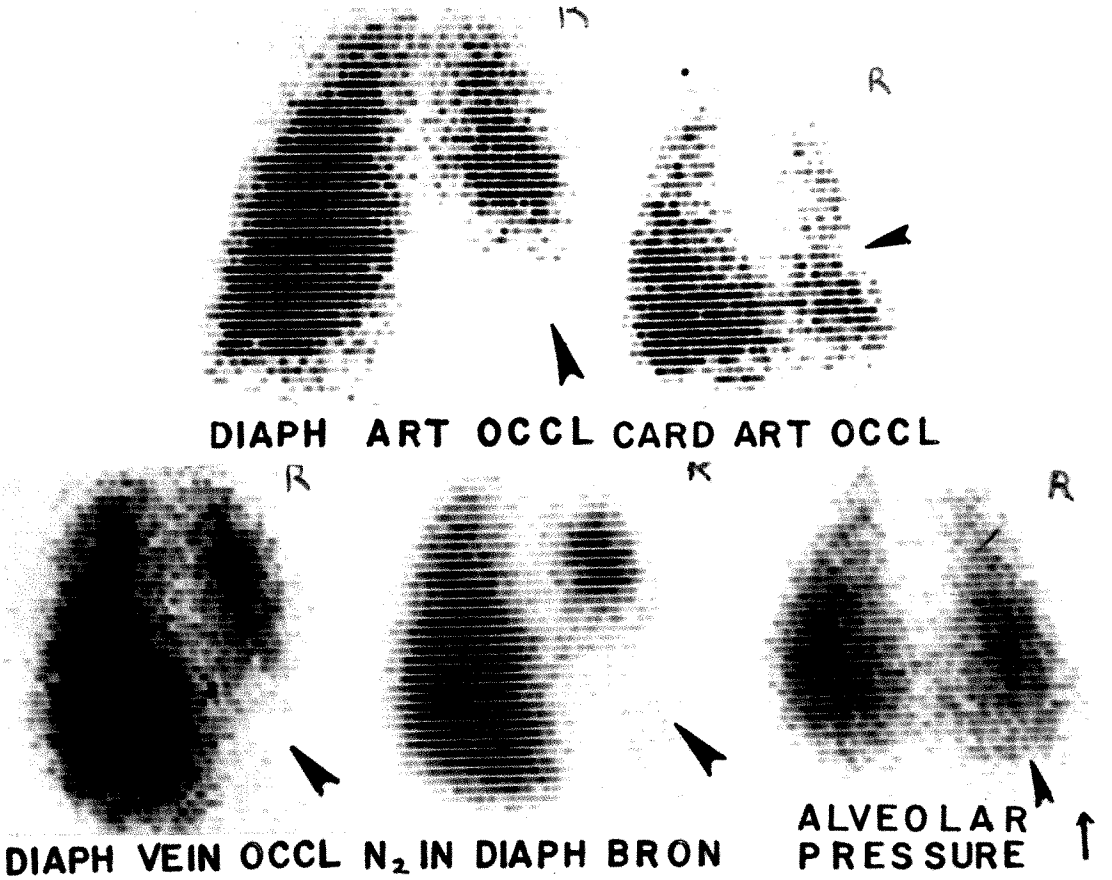


FIG. 1. Defects seen on perfusion lung scans in mongrel dogs after occlusion of cardiac or diaphragmatic lobe vessels, artificial bronchial hypoxia or overinflation.

The true incidence of this disease is not known, but it has been agreed that since Virchow's time it's greater than we think. The clinical spectrum ranges from no signs or symptoms all the way to sudden and unexpected death.

In many series the finding of Hampton and Castleman that at least 1/3 of the cases are in individuals without heart disease, and who are not postpartum or postsurgical, has been confirmed.

The clinical course of this disease is being worked out today. It does appear that most patients with emboli do not have infarct and suffer no sequelae. It is also becoming more apparent that close to 1/2 of patients with pulmonary emboli have their initial episode outside the hospital.

One more difficulty in establishing the prevalence of pulmonary emboli is the inadequacy of many postmortem examinations. The simple introduction of postmortem pulmonary angiography in one series resulted in a five-fold increase in embolic discovery and localization.[17]

In the 19th Century, Virchow listed the major states which predispose to venous thrombosis and possible pulmonary embolus as stasis, venous trauma and a hypercoagulable state. This has not changed substantially to date.

The acute catastrophe of massive pulmonary embolus requires speedy diagnosis and effective treatment. There is little that one can do for the massive embolic case with sudden clinical death. Resuscitation is extremely difficult unless embolectomy can be performed immediately. This would, of course, require that the embolus occurred under optimal treatment circumstances.

Those patients with massive embolus who survive for several hours, teetering precariously at death's door, are a group where lung scanning can play a significant role in their diagnosis and management. The clinical picture in these cases can mimic myocardial infarct[16] and cause undue delay in treatment. The lung scan is extremely useful in selecting suspect massive embolus patients for the definitive diagnostic procedure, the pulmonary angiogram. If the scan is normal, a recent massive pulmonary embolus up to the time of injection of the radioaggregate is excluded and angiography is unnecessary. If the scan is abnormal, then angiography is required to confirm the diagnosis and should be a *sine qua non* if embolectomy is anticipated. The use of a lung scan to select candidates for angiography when massive embolus is suspected can only be justified if the procedure can be performed immediately. With detector systems available today, this information *can* be acquired innocuously in a matter of minutes.

In cases of large pulmonary embolus without infarct, the restoration of capillary blood flow to normal can occur in as little as 48 hours. Because of this, the lung scan may be normal while the pulmonary angiogram is still abnormal if there is a 2 to 3 day delay in performing the scanning. The converse may also occur if vessels no larger than 1–2 mm. are occluded. Arteries of this size may supply a portion of lung with a 1–2 inch pleural diameter.

Smaller emboli are probably the most common and most difficult to diagnose pulmonary embolic phenomena. The necessity for minimal delay in performing scannings is even more critical in these cases.

In following the course of pulmonary emboli with serial lung scans, change is the rule rather than the exception. What is often surprising is that these changes, probably due to new emboli, may occur under what is considered adequate anticoagulation.

The concept of suspended judgment in perfusion lung scanning is important. A repeat study is frequently required in order to separate pulmonary embolism or infarct from other conditions which cause altered perfusion. Within 2 to 4 days, even in pulmonary infarct, there will be changes in the perfusion pattern which strongly support a pulmonary embolus diagnosis. This suspended judgment is no less necessary in lung scanning than it is in roentgenology. Dr. George Holmes, in commenting on Hampton and Castleman's presentation, noted "A single examination may be negative and we should be given the opportunity to examine these patients more than once and on different days."

There have been several ways suggested to circumvent this delay: by imaging both the ventilation and perfusion spaces simultaneously; by recording the increased physiologic dead space which accompanies acute pulmonary embolus. The combination of aerosol and perfusion scannings is not entirely satisfactory. A more accurate method would combine a true ventilation space recording using the camera and a radioactive gas (xenon 133) along with perfusion macroaggregate scanning.

HILAR COMPRESSION

Pulmonary artery or vein compression by masses in the mediastinum or by pleural effusion will also alter pulmonary perfusion, as will abnormal pulmonary vascular pressures and oxygen content.

When tumors are located at the left hilum, the pulmonary blood flow to that lung may be greatly disturbed. This is thought to be due to the fact that bifurcation of the left pulmonary vessels takes place more distally than does the right, and that the left pulmonary artery or vein is more liable to external compression by tumor or enlarged lymph nodes. If bilateral defects at the hilum are seen, resectability is much less likely.

EFFUSIONS

Until the free pleural effusion reaches approximately 1,500 cc. in quantity, the intrathoracic pressures are unchanged and the lung scan will be normal. If the patient is injected in the sitting position, the free

fluid gravitates to the base and will compress the lower portion of the lung resulting in a scan defect (Fig. 2*A*). It is for this reason that we inject patients in the recumbent position (Fig. 2*B*).

Pulmonary venous hypertension will also occasion abnormal perfusion, with increased flow to the upper lobes and decreased to the lower lobes. The depiction and quantitation of this phenomenon by perfusion lung scanning was first performed by Friedman and Braunwald[2] and later confirmed in our laboratory.[18]

The ratio of counts in the upper to midlung in the right lung correlates well with the pulmonary arterial and left atrial pressures and inversely with cardiac output. The presence of idiopathic pulmonary hypertension, but not its severity, can be determined. Caution should be exercised in interpreting these results when emphysema, congestive heart failure and pulmonary emboli concomitantly exist.

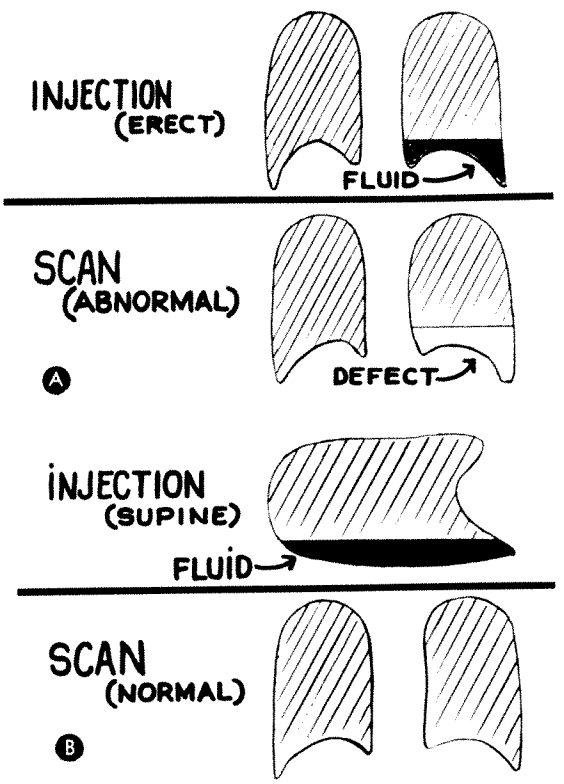


FIG. 2. (*A*) In the erect position, free fluid gravitates to the diaphragmatic surface and compresses the lower lobe resulting in a perfusion defect. (*B*) This can be obviated by the distribution over a greater area of the fluid in the supine position. When scanned posteriorly with the patient in the prone position, the lung floats closer to the detector and the scan may be normal.

Alveolar hypoxia, due to bronchial tumors or mucus plugs or blood in the bronchus, will decrease pulmonary perfusion to those areas. Inhalation scans will depict absent aerosol deposition or absent gas flow and help separate these conditions from pulmonary embolus. Alveolar hypoxia, secondary to mucus plugs, may be the reason why so many postoperative nonembolic patients have abnormal lung scans. It may also be one of the major reasons why patients with asthma have multiple defects which are not present after the acute attack has resolved. Recent reports suggest, however, that hyperinflation of the lung may be more important in causing hypoxemia in asthmatics than obstruction to bronchial air flow.[10]

EMPHYSEMA

Bullous emphysema causes large defects on both the perfusion and the inhalation scans. This may offer useful information if bullectomy is planned.

Centrilobular emphysema, almost always associated with chronic inflammation, occurs most often in the upper and lateral zones of the lung and varies in severity from area to area. Panlobular or panacinar emphysema is found most frequently in the anterior basal segments and lower zones. In far advanced cases these two different types frequently co-exist. Correlation of conventional chest roentgenograms, and physiologic observation with anatomic status remains poor. Lung scanning may help to distinguish these two types of emphysema which would aid in prognosis if not in therapy.

SUMMARY

The technology which brought us lung scanning challenges our ability to properly use the procedure in uncovering our ignorance, reshaping our thoughts and translating them to better patient care.

Lung scanning represents a challenge to

Nuclear Medicine on several fronts. It is a challenge to ourselves to become expert in the current knowledge of pulmonary pathophysiology. It is refreshing, although rare, to see pulmonary basic science discussed adequately in articles on lung scanning. A further challenge is for us to improve our diagnostic technique at all levels. Our radiopharmaceutical preparation is far from ideal. We need better quality control of particle size, perhaps through the recently discovered metabolizable microspheres to which radionuclides are adsorbed;[18] and an improvement of our detecting crystals, replacing the tried, tested, satisfactory but not ideal sodium iodide. Encouraging work on lead fluoride crystals may be a part of our much needed instrument break-through. The penchance for camera *versus* scanner dialogue should be very quickly brought to an end and a clear definition of the advantages one to the other should be stated, accepted and applied. Uniformity of read-out should be sought. Scanning is still in that unmanageable infant state where one laboratory finds the interpretation of another laboratory's scanning unacceptable.

The final challenge is in the area of communication: communication not only with a medical colleague in other clinical disciplines, but also our colleagues in the physical science disciplines through common colloquia, comparing information with information.

If we are not responsive to these challenges, we will deserve the severe admonition which Marshall McLuhan refers to as " . . . the witless repetitive response to the unperceived," or, at best, the gentle exclamation Dr. Hampton would occasionally make to his residents, "How can you be so ignorant!"

Department of Nuclear Medicine
Chicago Wesley Memorial Hospital
250 East Superior Street
Chicago, Illinois 60611

REFERENCES

1. CARR, E. A., JR., BEIERWALTES, W. H., WEGST, A. V., and BARTLETT, J. D., JR. Demonstration of myocardial infarcts by photoscanning. *J. Nuclear Med.*, 1962, *3*, 199.
2. FRIEDMAN, W. F., and BRAUNWALD, E. Alterations in regional pulmonary blood flow in mitral valve disease studied by radioisotope scanning: simple nontraumatic technique for estimation of left atrial pressure. *Circulation*, 1966, *34*, 363–376.
3. GOOCH, A. S., MARANHAO, V., ALBLAZA, S., and GOLDBERG, H. Medical complications following open-heart surgery. *A.M.A. Arch. Int. Med.*, 1967, *120*, 672–678.
4. HAEGELIN, H. F., and MURRAY, J. F. Means of distinguishing pulmonary emboli and other causes of pulmonary hypertension. *Dis. Chest*, 1968, *53*, 138–147.
5. HAMPTON, A. O., BICKHAM, C. E., JR., and WINSHIP, T. Lipoid pneumonia. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1955, *73*, 938–949.
6. HAMPTON, A. O., and KING, D. S. Middle lobe of right lung: its roentgen appearance in health and disease. AM. J. ROENTGENOL. & RAD. THERAPY, 1936, *35*, 721–739.
7. HAMPTON, A. O., and ROBINSON, J. M. Roentgenographic demonstration of rupture of intervertebral disc into spinal canal after injection of lipiodol. AM. J. ROENTGENOL. & RAD. THERAPY, 1936, *36*, 782–803.
8. HAMPTON, A. O., and CASTLEMAN, B. Correlation of postmortem chest teleroentgenograms with autopsy findings: with special reference to pulmonary embolism and infarction. AM. J. ROENTGENOL. & RAD. THERAPY, 1940, *43*, 305–326.
9. MEIER-EWERT, K., BAUMGART, H. H., and FRIEDENBERG, P. Thromboembolic complications of psychopharmaceuticals. *Deutsche med. Wchnschr.*, 1967, *92*, 2174–2178.
10. PALMER, K. N. V., and DIAMENT, M. L. Hypoxaemia in bronchial asthma. *Lancet*, 1968, *1*, 318–319.
11. QUINN, J. L., III, WHITLEY, J. E., HUDSPETH, S. A., and WATTS, F. C. Approach to scanning of pulmonary infarcts. *J. Nuclear Med.*, 1963, *4*, 200.
12. QUINN, J. L., III, WHITLEY, J. E., HUDSPETH, S. A., and WATTS, F. C. Approach to scanning of pulmonary infarcts. *J. Nuclear Med.*, 1964, *5*, 1–8.
13. QUINN, J. L., III, WHITLEY, J. E., HUDSPETH, A. S., and PRICHARD, R. W. Early clinical applications of lung scintiscanning. *Radiology*, 1954, *82*, 315–317.
14. QUINN, J. L., III, and WHITLEY, J. E. Lung scintiscanning. *Radiology*, 1964, *83*, 937–943.
15. RHODES, B. A., ZOLLE, I., and WAGNER, H. N., JR. Properties and uses of radioactive al-

bumin microspheres. *Clin. Res.*, 1968, *16*, 245.

16. SASAHARA, A. A., CANNILLA, J. E., MORSE, R. L., SIDD, J. J., and TREMBLAY, G. M. Clinical and physiologic studies in pulmonary thromboembolism. *Am. J. Cardiol.*, 1967, *20*, 10–20.
17. SMITH, G. T., DAMMIN, G. J., and DEXTER, L. Postmortem arteriographic studies of human lung in pulmonary embolization. *J.A.M.A.*, 1964, *188*, 143–151.
18. STEINER, S. H., and QUINN, J. M., III. Cardiovascular hemodynamics: determination from distribution of pulmonary blood flow in seated patients. *J.A.M.A.*, 1968, *203*, 850–856.
19. STERN, H. H., GOODWIN, D. A., WAGNER, H. N., JR., and DRAMER, H. Indium-113m: short-lived isotope for scanning. *Nucleonics*, 1966, *24*, 57–59.
20. TAPLIN, G. V., JOHNSON, D. E., DORE, E. K., and KAPLAN, H. S. Gastric photoscans with colloidal aggregates of radioalbumin: mechanism, diagnostic and therapeutic implications. *J. Nuclear Med.*, 1963, *4*, 193.
21. WESSLER, S., and AVIOLI, L. V. Anticoagulants in treatment of patients with hip fracture. *J.A.M.A.*, 1968, *204*, 140–144.
22. WHITLEY, J. E., QUINN, J. L., III, HUDSPETH, A. S., and PRICHARD, R. W. Scintiscanning of experimentally produced pulmonary infarcts. *Radiology*, 1963, *81*, 884–885.

PRECISE ALIGNMENT OF X-RAY BEAMS FOR STEREOTACTIC SURGERY*

By PAUL C. HODGES, M.D., *and* FRANCISCO GARCIA-BENGOCHEA, M.D.
GAINESVILLE, FLORIDA

WITH at least one important exception[4] the X-ray guidance of neurosurgical instruments usually has been done at tube-film distances of 2 meters, 3 meters, or more, alignment being accomplished by means of light beams attached to the housings of the X-ray tubes.[1] Time is saved, cost reduced and accuracy improved if tube-film distance is reduced to 1 meter and alignment is done with the X-ray beams themselves (Fig. 7; 8, *A* and *B*; and 9, *A* and *B*). We have devised an apparatus of this sort for thalamectomy and have used it successfully in over 20 operations. The construction, alignment and surgical employment of the apparatus are described in the text of this article and the legends for its 12 figures.

GEOMETRY OF STEREOTAXIS

When the patient's head has been fixed in an instrument-guidance system, oriented so that its geometric center coincides with the crossing of frontal and lateral X-ray beams, preliminary roentgenograms are made. In the lateral film the image of the anatomic target on the thalamus is computed from the location of the image of the junction of the middle and posterior thirds of the intercommissural line, and in the frontal film by measurement from the midline of the brain. Almost invariably the first films will show the image of the target displaced more or less from the center of the guidance system, but because of the fact that X-rays diverge from their source, the magnitude of that displacement will be greater than the displacement of the anatomic target itself. Figure 2 shows the geometry for the frontal beam and film, but the mathematics are the same for the other plane. The magnitude of displacement of the anatomic target (T) from the longitudinal axis of the frontal film (L) is designated "O" (object) and the displacement of its image (I.T.) is designated "I" (image). When the measured values of "O" and "I" are substituted in the familiar equations for the divergent distortion correction factor and its reciprocal, we acquire tools for computing the location of the image of the thalamic target relative to the midline of the brain and for determining the net amounts by which head and beam-reticle assembly must be shifted to bring the target to the geometric center of the instrument-guidance system (Fig. 11, *A* and *B*; and 12, *A* and *B*). Regardless of the magnitude of tube-film distance these computations must be made, and the fact that with longer distances the correction factor becomes more nearly 1.0 has no practical advantage. Long distances, however, have serious mechanical disadvantages plus the disadvantage of requiring much heavier X-ray tube loading.

APPARATUS

We employ a modification of the Todd-Wells head-holder, instrument-guidance system[5] (Fig. 3; 4; and 5) mounted on the optical bed (Fig. 6) of a beam aligning unit of our own design (Fig. 1). Two small X-ray generators are carried on a sturdy tubular steel "bridge" running on precisely aligned optical rails so that it can be rolled out of the surgical field except for the period of film exposure. A bracket on the bridge carries a feeler gauge and when the X-ray beams are to be brought into posi-

* Presented on May 23, 1968 to the Wisconsin Medical Alumni, Madison, Wisconsin; and on August 30, 1968 to The Scandinavian Neurosurgical Society, Ahrus, Denmark.

From the Department of Radiology and Department of Surgery (Division of Neurosurgery), University of Florida, College of Medicine, Gainesville, Florida.

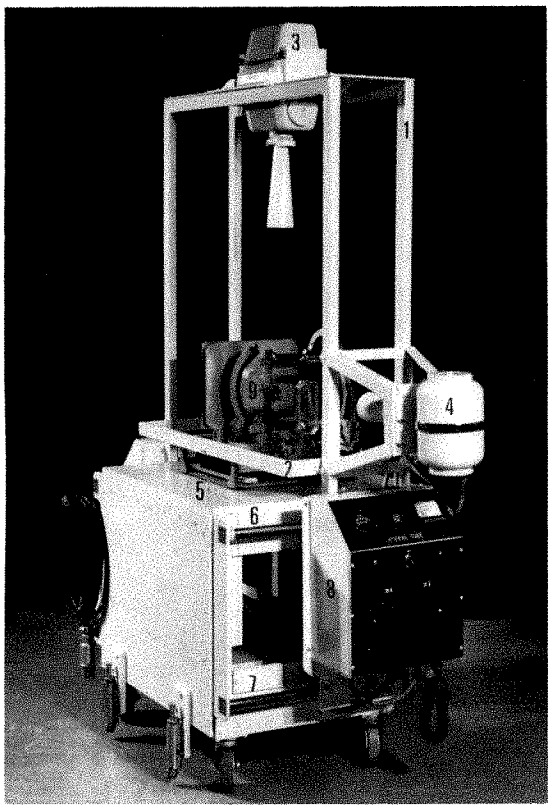


Fig. 1. General view of apparatus. 1. Bridge; 2. Bracket; 3. Frontal X-ray generator and its collimator; 4. Lateral generator and its collimator; 5. Optical bed; 6. Upper optical rail; 7. Lower optical rail (there are 2 similar rails at the other side); 8. Control for lateral generator;* 9. Plastic reticles supplied by manufacturer of head holder. We substitute magnesium reticles (see Fig. 4).

Wheeled base, bridge, X-ray generators and their collimators and controls constitute a unit which can be moved through standard hospital doors including elevator doors. Between periods of service it can be draped with a protective cover and stored in corridors or apparatus storage rooms. The instrument guidance system, including head holder and "far" reticle, is wrapped in cloth and gas sterilized and when unwrapped in the operating room is placed down on the optical bed "registered" in place by means of 2 dowels (see Fig. 6). The unit is not safe for use with explosive anesthetics, but our surgeons and anesthesiologists are content to work only with the nonexplosive variety.

With a phantom head in position and the frontal tube operating at 80 kv., 10 ma., the dose at 2 meters is only 0.2 mr/min. and for the lateral tube operating at 75 kv. and 12 ma., the dose is 1.0.

* Generator and control are the greatly appreciated gift of a friend who prefers to remain anonymous.

tion for filming, the surgeon has merely to see to it that the tip of the gauge touches the back of the "horseshoe" of the instrument guidance system in order to assure that the crossing of the 2 beams lies at the geometric center of the head-holder assembly. The reticle, a silver-filled grating ruled into a sheet of magnesium (Fig. 4), is permanently mounted on the head-holder so that its center point lies on the transverse axis exactly opposite the geometric center of the guidance system when the bridge is in filming position. A silver-filled line in the magnesium holder for the frontal film defines the longitudinal axis of that film and is centered exactly beneath the center of the frontal X-ray beam.

The complete apparatus has over-all dimensions of only 24×60×74 inches in height. It is carried on rubber tired casters, will pass through standard hospital doors and can be wheeled into whatever operating room is available to the surgeon. It is not safe for use near explosive gasses, but of course explosive anesthetics are not necessary for this type of surgery.

SURGICAL DETAILS

To be used, the apparatus is wheeled into position at the end of a standard operating table, clamped to it, and floor locks set (Fig. 10). The sterilized assembly of base, horizontal arc, 2 film holders and fixed reticle of the head-holder guidance system are placed on the optical bed, being precisely located there by 2 dowels (Fig. 6). Finally, the patient's head is anchored to the head-holder.

VENTRICULOGRAPHY

For the roentgenologic identification of landmarks we use a modification of the

These very low doses are accomplished by close collimation of both beams and lead backing on both cassette holders. Since individual films require exposures of only 3–5 seconds, it is merely necessary for doctors, nurses and technicians to step back to a distance of 2 meters from the patients head in order to work safely without leaded aprons, gloves or protective screens.

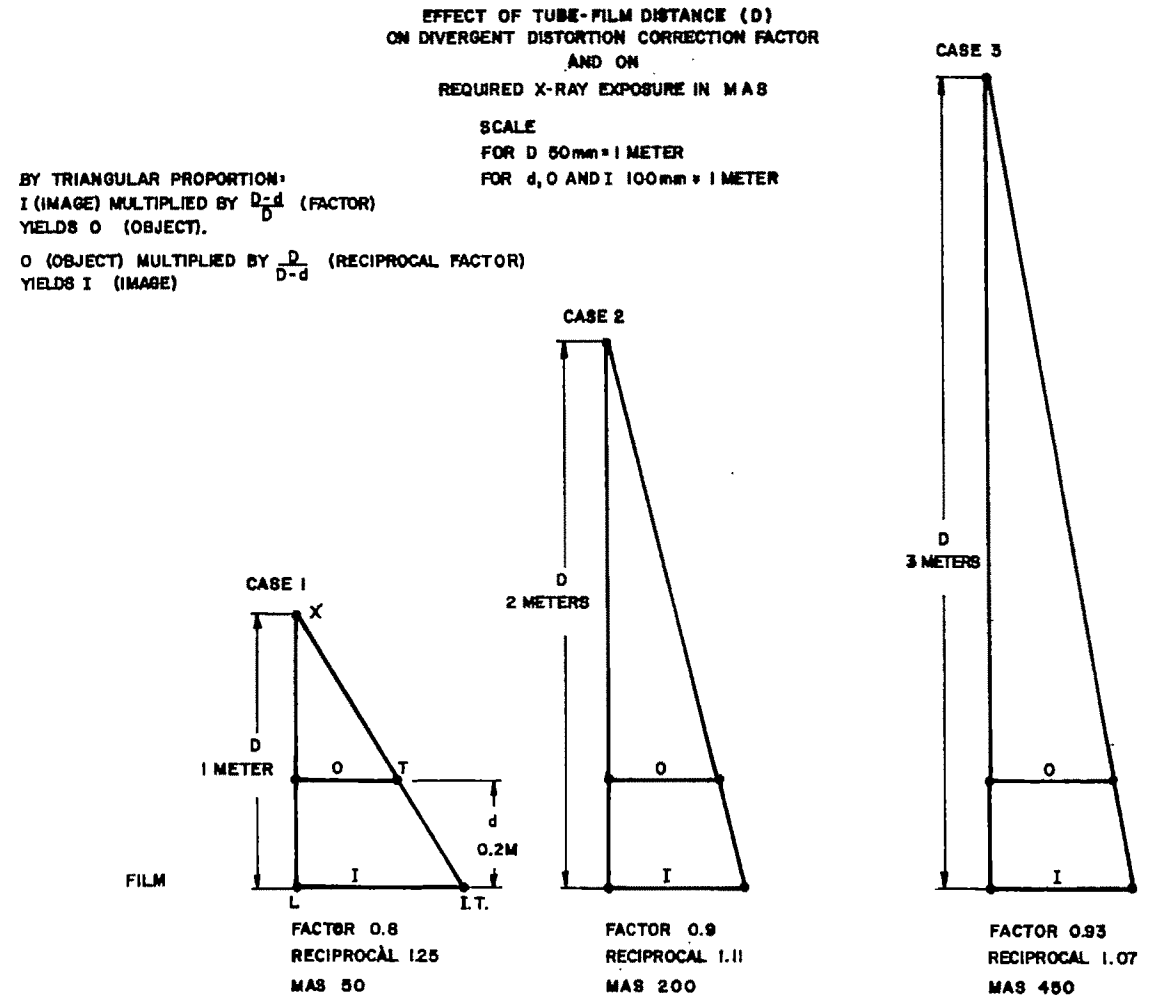


FIG. 2. Geometry. X = Target of frontal X-ray tube; L = Longitudinal axis of frontal film; D = Tube-film distance; T = Anatomic target; d = Distance of anatomic target above film; O = Displacement of target from axis of film; I.T. = Image of target; I = Displacement of image from axis of film. In Case 1, D = 1 meter; Case 2, D = 2 meters; Case 3, D = 3 meters. If the scale had been 50 mm. = 1 meter for all values, T would be shown lying only 10 mm. above the film and 10 mm. displaced from the longitudinal axis, and I. T. would lie only 12.5 mm. away from the film axis. Instead, a scale of 100 mm. = 1 meter has been used for all values other than D. The use of 2 scales distorts the geometry so that *measurement* of I on the drawing is not significant, but the distortion makes the geometry more obvious.

As D increases from 1 meter to 2 and then 3 meters, "O" and "I" differ less and less, the correction factor becoming larger and its reciprocal smaller. However, accuracy rests not on the magnitude of correction factors but rather on the precision with which the 2 X-ray sources have been lined up perpendicular to their respective films and intersecting one another exactly at the geometric center of the instrument guidance system. Such alignment is easier and more precise when D is 1 meter, more difficult and less precise as the magnitude of D increases. Furthermore, because of the inverse square law, the mas. required at a D of 1 meter must be quadrupled at 2 meters and increased nine fold at 3 meters.

This drawing portrays the frontal tube and film, but the geometry is identical in the case of lateral tube and film. The application of this simple geometry is explained in connection with Figures 11 and 12.

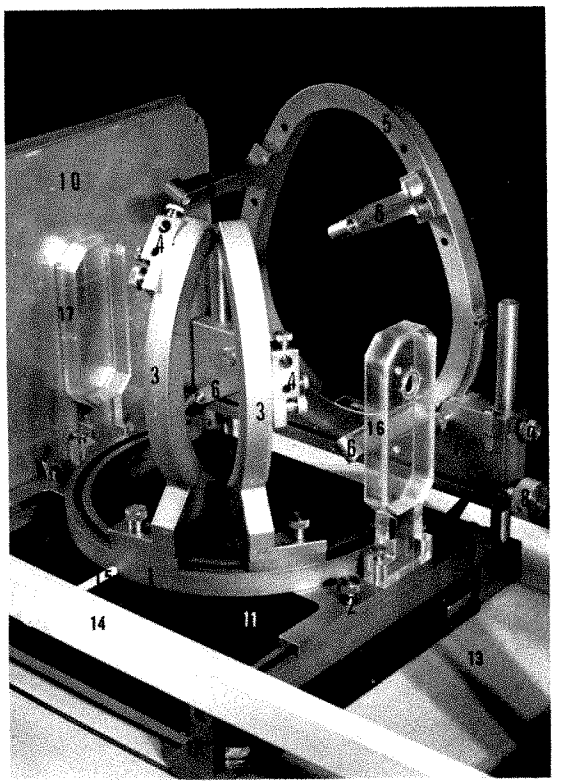


FIG. 3. Todd-Wells head holder and instrument guide. 1. "Horseshoe"; 2. Base lock; 3. Instrument guide arcs; 4. Instrument guide riders; 5. "Crown" for immobilizing patient's head; 6. Supports for immobilizing pins; 7. Support in which "crown" is clamped; 8. Pinion for moving patient's head ventrally or dorsally; 9. Lock to arrest such movement; 10. Lateral cassette holder; 11. Frontal cassette holder; 12. Base of Todd-Wells device; 13. Optical bed of our apparatus; 14. Bracket on bridge; 15. Feeler gauge on bracket. The tip of the gauge is in contact with the "horseshoe" as it must be when films are to be exposed; 16. "Near" reticle, so-called because it lies nearest to the source of radiation. This original reticle of clear plastic has inherent disadvantages and we have replaced it with one made of sheet magnesium (see Fig. 2); 17. "Far" reticle of clear plastic. This too has been replaced by sheet magnesium (see Fig. 2).

For all positions of arc and rider a freezing instrument introduced through a hole in the rider and advanced until its tip is 135 mm. beyond the back of the rider will lie with its tip at the midpoint of an imaginary line joining the centers of the 2 lateral reticles and directly over the longitudinal axis of the frontal film.

The objective of all the maneuvers presently to be described is to identify an anatomic target in the brain and bring it exactly to the geometric center of the guidance system so that a freezing instrument introduced through a hole in a rider will lie with its tip exactly at that target.

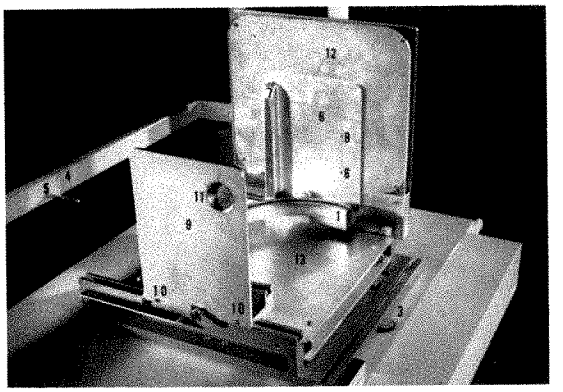


FIG. 4. Magnesium reticles. 1. Horseshoe; 2. Base; 3. Optical bed; 4. Bracket; 5. Feeler gauge; 6. "Far" reticle of 1/32 inch sheet magnesium; 7. Strengthening rib at edge, outside the field of examination; 8. Holes for screws that hold jig during optical alignment of frontal X-ray beam (see Fig. 7); 9. "Near" reticle (used only during preliminary optical alignment of the 2 X-ray beams) is 1/32 inch sheet magnesium cemented to a sheet of 1/4 inch aluminum for rigidity; 10. Screws which attach reticle to "horseshoe"; 11. 1 1/4 inch opening through aluminum at site of reticle; 12. Lateral cassette holder with built-in stationary grid; 13. Frontal cassette holder with built-in grid. A line engraved in the magnesium front and filled with silver* defines the longitudinal axis of the 8×10 inch frontal film.

The original plastic reticles were somewhat unstable dimensionally and the reinforced margins showed on films and sometimes obscured landmarks. Both had to be used for each examination and beam alignment had to be checked from time to time during the course of examinations. With our apparatus and our modifications of the head holder and instrument guidance system the "far" reticle remains in position at all times and the "near" one is unused once beam alignment has been accomplished.

This part of the guidance system is clamped to the bed of a milling machine and before the reticles are engraved their centers are located. These centers lie on an imaginary line perpendicular to the lateral film and with its midpoint perpendicularly above the longitudinal axis of the frontal film. A similar technique (see Fig. 7) is employed for locating the shot and silver filled line in the magnesium jig for alignment of the frontal beam.

* Eccobond Silver-Epoxy Easy Mix #57-C Paste. Emerson & Cuming, Inc., Canton, Massachusetts.

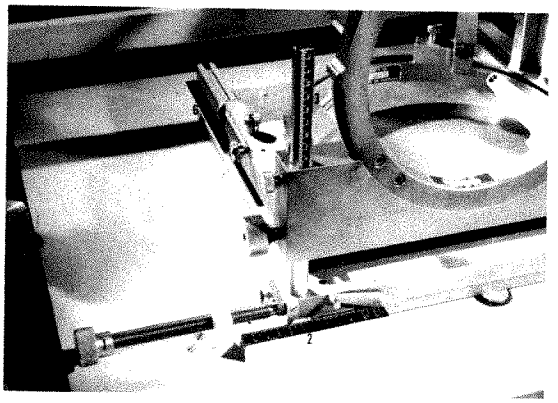


FIG. 5. Other modifications of Todd-Wells device. 1. Screw for transverse movement of patient's head; 2. Scale for transverse movement; 3. Scale for ventral-dorsal movement of head; 4. Pinion for shifting horseshoe and attached "Far" reticle toward vertex or toward feet; 5. Lock for such motion; 6. Scale for such motion.

The original scales were engraved in metal and hard to read. Ours are easily readable being engraved on black plastic laminated on white backing. Transverse shifting of the head formerly was done by pushing or hammering the base of the yoke along its ways. We accomplish this motion with a screw. Shifting of reticle and horseshoe assembly toward feet or toward vertex we do by means of a rack and pinion rather than by pushing or hammering. In the locks for the slotted ways in base, horseshoe and guidance arcs (see Fig. 3) the small rectangular clamping members at the ends of locking screws were free to rotate until they had been lodged within their slots. As a result a surgical assistant, in sterile attire, assembling the sterilized parts of the guidance system wasted much time maneuvering the rectangles into their slots. The difficulty has been corrected by fixing small pins in the clamps. These pins ride in free fitting holes in the blocks into which the screws are tapped, preventing the rectangles from rotating out of alignment with their respective slots.

method of positive pressure ventriculography described by Calvin and Coe.[2] We make the burr hole on the day of the stereotactic procedure, after the patient has been fixed in the holding and guiding apparatus, and place the hole on the coronal suture, 3 cm. from the midline. Usually no fluid is removed except for the few drops lost in ascertaining that the ventricle has been entered, and in connecting rubber tubing to the brain cannula. For adults without increased intracranial pressure 15 cc. of air is injected gently in 40 to 60 seconds and the first films (lateral and anteroposterior) are exposed (Fig. 11, *A* and *B*; and 12, *A* and *B*). If the films reveal that more air is needed, it is added in small increments according to estimates based on pressure levels and the degree of ventricular filling already obtained. For thalamectomies adequate visualization of the third ventricle and rostral aqueduct of Sylvius usually is achieved with volumes of air ranging from 20 to 30 cc. In some cases it may be necessary to remove some fluid and inject larger amounts of air, the optimum volume of air seeming to be related to atrophy and ventricular size.[3] During the injection of air

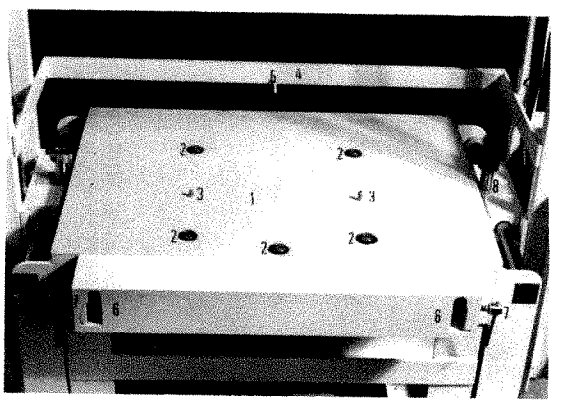


FIG. 6. Optical bed. 1. Bed; 2. Pads; 3. Dowels; 4. Bracket; 5. Feeler gauge; 6. Slots to receive brackets on operating table; 7. Locks to anchor operating table to apparatus; 8. Locks to fix bridge to optical rails.

The bed is 5/8 inch in sheet aluminum bolted to the steel table top, the latter having been machined to be flat and as nearly as possible perpendicular to the 2 machined sides which carry the supports for the 4 optical rails. To further increase accuracy the head holder rests not on the aluminum top but rather on 5 brass "pads" which are threaded into the aluminum and project through the sheet plastic which is cemented to it. By means of surface gauges these pads are raised and lowered until they are within 3 thousandths of an inch of defining a plane perpendicular to the planes of the optical rails. When the head holder has been placed down on the dowels, the longitudinal axis of the frontal film will lie directly beneath the source of the frontal X-ray beam for all positions of the bridge, and when the feeler gauge makes contact with the horseshoe both beams will intersect at the geometric center of the instrument guidance system.

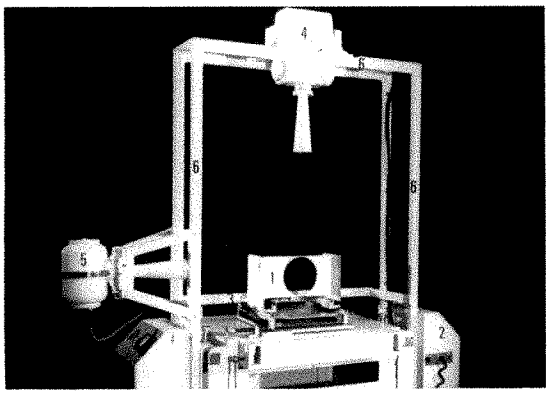


FIG. 7. Alignment of X-ray beams. A sheet of 1/4 inch magnesium (1) 6 inches wide, 12 5/8 inches long and with a 5 5/8 circular cut out in the center forms a jig for the alignment of the frontal beam. With the holder clamped to the bed of a milling machine (see legend Fig. 4) the jig is lined up with the centers of the 2 reticles. At the upper edge a small hole is drilled exactly over the longitudinal axis of the frontal film and in the lower edge a short groove is milled out exactly parallel with the imaginary line connecting the 2 reticle centers and perpendicularly beneath the hole in the upper edge. A small "shot" (actually a ball bearing) is pressed into the hole in the upper edge of the jig and silver-epoxy paste applied to the groove, thus providing two landmarks for optical alignment of the frontal X-ray beam (see Fig. 8); (2) is the control for the frontal generator, (3) the bracket which supports the feeler gauge (in this view concealed by the jig), (4) is the frontal generator, (5) the lateral generator and (6) the tubular steel bridge on which the two generators are mounted. Alignment of the lateral beam is described in the legend for Figure 8. When both alignments have been made the 2 generators are locked in position and the jig and "near" reticle are removed and not used again.

The short tube-film distance of 1 meter in every way improves and in no respect decreases the accuracy of instrument guidance. Because at 1 meter an exposure of 50 mas. suffices, the generators may be small and of light weight so that they can be carried on a tubular steel bridge which allows no significant sag. Once alignment has been accomplished nothing short of a serious mechanical accident will disturb it. The fact that divergent distortion of images is greater than it is at greater "D's" *improves* accuracy by magnifying the amount by which an anatomic target fails to lie at the geometric center of the guidance system. Errors in "d" and in the simple arithmetic required have no effect on accuracy and can merely increase somewhat the number of test films that must be made. Once a target lies at the geometric center all other factors have been eliminated and beam alignment alone affects accuracy.* To be true the diameter of the image of the target will be larger than the target itself but since we are dealing with the center of that image its actual diameter is of no importance whatever.

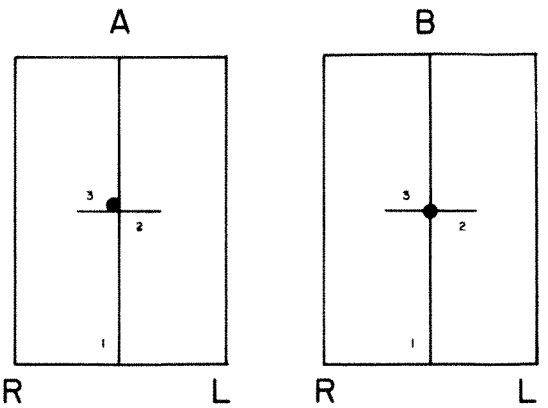


FIG. 8. Optical alignment of frontal X-ray beam. 1. Image of silver filled line in frontal cassette holder indicating longitudinal axis of frontal film; 2. Image of short, transverse, silver-filled line at lower edge of jig; 3. Image of small shot imbedded in upper edge of jig. (*A*) This drawing from a film early in a series of tests shows the shot displaced slightly above and to the left of the central crossing of film axis and transverse line. (*B*) Following a test series, with appropriate shift of frontal tube between tests, the shot is found to lie precisely at the central crossing of transverse line and film axis. The precision of this type of alignment is much greater than the best that could be accomplished with light beams and once such alignment has been done it need never be done again.

In the films themselves the images of shot and transverse line, even though superimposed on the magnesium forming the upper and lower portions of the cut-out in the jig, could be well seen by transmitted light. Because such films do not lend themselves well to reproduction we have employed for this figure not film reproductions but an artist's drawing made from the films.

* Except for computation of location of image of target in frontal film (see Fig. 11).

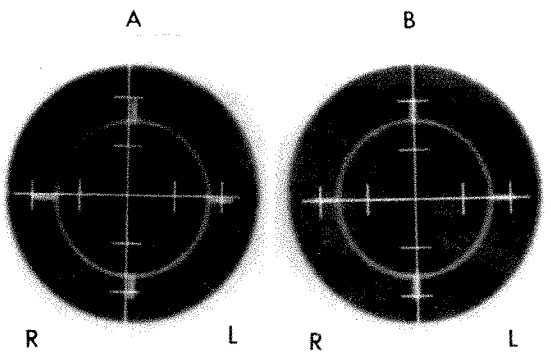


FIG. 9. Optical alignment of lateral X-ray beam. By means of skillful and painstaking machine work (see Fig. 4 and 7) the centers of the 2 reticles are made to lie so that an imaginary line connecting them is exactly parallel with the frontal film and perpendicular to the lateral film. When this has been done and the lateral tube arranged with its target approximately in line with the 2 reticle centers, further tube alignment is accomplished by optical means. The "far" reticle has silver-filled vertical and transverse lines each with four transverse strokes. The "near" reticle consists of a silver-filled circle with strokes at IX, XII, III and VI o'clock. (*A*) The near reticle is displaced downward and to the left relative to the far reticle indicating that the target of the lateral tube is in not quite perfect alignment. (*B*) After repeated tests, with shift of X-ray tube between them, the 2 reticles coincide. The tube is now locked in position and the "near" reticle removed. It is used merely for this preliminary alignment and clinical work employs merely the "far" reticle which remains permanently in place. The beam alignment illustrated here and in Figure 8 assures that the 2 beams meet at the geometric center of the instrument guidance system.

and the making of roentgenograms, care is taken to prevent loss of pressure and to avoid introducing unnecessary air into the fourth ventricle.

SELECTION OF ANATOMICAL TARGETS AND BRINGING THEM TO THE CENTER OF INSTRUMENT GUIDANCE SYSTEM

Subject to subsequent correction based on physiologic response, the anatomic target is assumed to lie 13.6 mm. to the right or left of the midline and at a point 1 mm. rostral and 3 mm. dorsal to the junction of the posterior and middle thirds of the intercommissural line. When the first films (lateral and frontal) have been exposed following the injection of air, the "work-up" begins and continues through subsequent films until the target has been brought to the longitudinal axis of the frontal film and the center of the reticle in the lateral film. When these two objectives



FIG. 10. Apparatus attached to operating table. 1. Bracket on operating table enters receptacle on our apparatus; 2. Lock holds table bracket in place; 3. Frontal X-ray generator; 4. Lateral X-ray generator; 5. Bridge.

The 2 beams are closely collimated so that they cover a mere 6 inch circle at the films and both cassette holders are backed with lead. As a result, the output of scattered radiation is so low that doctors, nurses, technicians and others working in the operating room do not need aprons or gloves (see Fig. 1).

At our institution surgeons and anesthesiologists have agreed to use only nonexplosive anesthetics, whenever surgery requires the employment of X-rays. Accordingly this apparatus, like all the rest of our X-ray apparatus, carries a sign stating that it is not safe for use in explosive atmospheres.

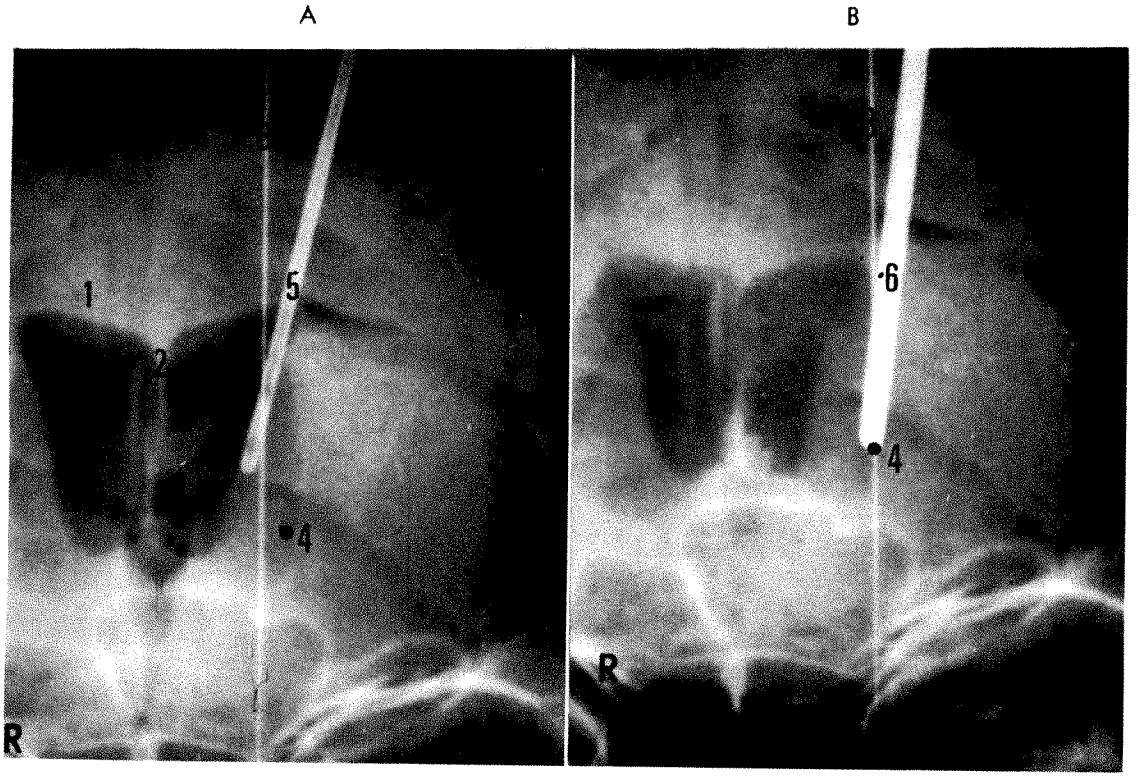


FIG. 11. Work-up of frontal film. In the average adult it has been found that the anatomic target in the thalamus lies 13.6 mm. lateral to the mid-line of the brain. Multiplying 13.6 by the reciprocal factor 1.25 (see Fig. 2) we obtain the value 17 mm. as the location of the image of that target lateral to the mid-line of the brain. This value remains the same throughout the film series and we treat a mark made on the film 17 mm. lateral to the mid-line of the brain as though it were the image of a visible structure. For example, if in a particular film that mark is found to lie 10 mm. to the left of the axis of the frontal film, we multiply that value by the correction factor 0.8 obtaining 8.0 mm. as the amount by which the patients head should be shifted toward the right.

1. Air-filled lateral ventricles; 2. Septum pellucidum; 3. Longitudinal axis of frontal film; 4. Mark placed on film indicating computed location of anatomic target; 5. Cannula for injection of air; 6. Freezing instrument.

(*A*) The target (4) lies slightly to the left of the longitudinal axis. (*B*) After several film exposures, with transverse shift of patient's head between them, the target (4) lies squarely on the longitudinal axis and the tip of the freezing instrument (6) coincides with it.

Note: It must be admitted that the ability to compute the location of the image (4) involves accurate knowledge of (d) and of the reciprocal factor (see Fig. 2) but clinical results in more than 20 operations indicate the soundness of the assumptions involved (see Fig. 7).

have been accomplished, the target will have been brought to the center of the instrument-guidance system. For details of working-up frontal and lateral films see the legends for Figures 11 and 12.

Physiologic testing is carried out by conventional means and, if necessary, final slight adjustments are made in the position of head and tube-reticle assembly. The remaining steps of the thalamectomy follow techniques which have been described by others and need not be repeated here.

DISCUSSION

Objection has been raised that any system requiring fixation of the patient's head in the brow-up position (as in the Todd-Wells head-holder) prevents adequate distribution of contrast media, either liquid or gaseous, by making it impossible to

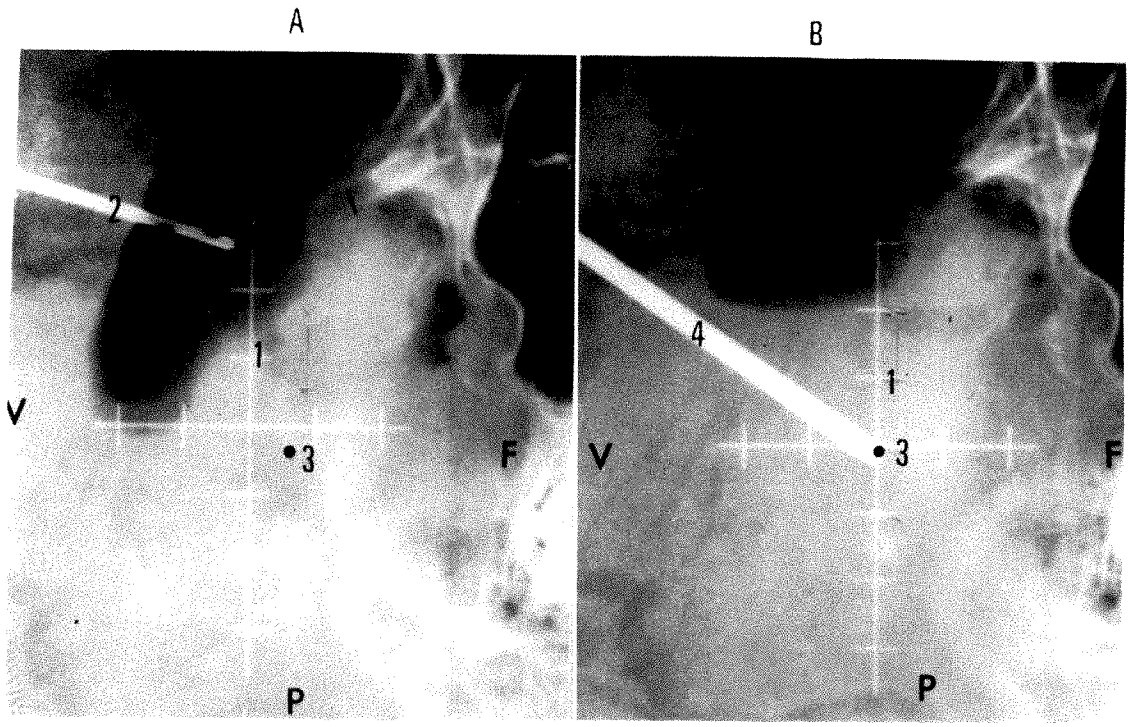


FIG. 12. Work-up of lateral film. (*A*) The anatomic target (3) lies posteriorly and toward the patient's feet relative to the center of the "far" reticle (1). (*B*) After several trial film exposures, between which patient's head was shifted anteriorly and the reticle-beam assembly toward his feet, the target (3) lies at the center of the reticle assuring that it is at the geometric center of the instrument guidance system. The freezing instrument (4) lies with its tip at the target, but before destructive freezing is done there must still be physiologic testing for further refinement of positioning.

The means of identifying the intercommissural line and locating the target 1 mm. rostral and 3 mm. dorsal to the junction of the middle and posterior thirds of that line are explained in the text.

move the head. Even previous to the development of our new equipment, however, we were convinced that the employment of positive pressure permitted consistent visualization of the third ventricle and aqueduct of Sylvius without moving the head from the brow-up position. We agree with Calvin and Coe[2] that with their positive pressure method there are fewer side effects than with standard ventriculography and pneumoencephalography, and we find it simpler than the method described by Clark *et al.*[3] Contrary to the suggestion by Waltz and Cooper[6] we believe that the tip of the cannula need not be placed caudal to the foramen of Monro in order to obtain consistent visualization of the posterior third ventricle, aqueduct, parts of both the fourth ventricle and basal cisterns in patients with patent ventricular and subarachnoid systems.

We attempt to prevent spread of air beyond the rostral fourth ventricle, not only to reduce side effects but also to avoid possible obscuration of the third ventricle and aqueduct of Sylvius by pockets of air in the subarachnoid space, but while we are not always successful in this attempt and air frequently is seen in the cisterns, in no case has it interfered with visualization of critical structures.

SUMMARY

1. Alignment of the X-ray beams used in stereotactic surgery is best done with those beams themselves rather than with light beams attached to the X-ray tube housings.

2. A tube-film distance of 1 meter is preferable to 2 or 3 meters or more, the shorter distance improving rather than diminishing the accuracy of localization of brain targets in thalamectomy.

3. In addition to improved accuracy, the short tube-film distance makes possible the use of small X-ray generators incorporated in a self-contained unit which can be wheeled into any operating room that happens to be available to the neurosurgeon at the moment.

4. Because the X-ray beams have been permanently aligned in the machine shop, the time for stereotactic surgery is remarkably shortened with resulting diminished discomfort to the patient.

5. The construction, calibration and surgical employment of such an apparatus are described.

6. Positive pressure ventriculography allows visualization of the third ventricle and the aqueduct of Sylvius in the recumbent patient.

Paul C. Hodges, M.D.
Department of Radiology
University of Florida
College of Medicine
Gainesville, Florida 32601

REFERENCES

1. Bailey, P. Chairman, Symposium on Stereotactic Surgery, Detroit, April 26, 1957. *J. Neurosurg.*, 1958, *15*, 239–280.
2. Calvin, T. H., Jr., and Coe, J. E. Positive pressure ventriculography for stereotaxic surgery. *J. Neurosurg.*, 1967, *26*, 548–552.
3. Clark, L., Moser, D., and Brackett, C. Controlled small volume ventriculography. *J. Neurosurg.*, 1966, *24*, 777–778.
4. Dobben, G. D., Mullan, S., and Moseley, R. D., Jr. New biplane neuroradiologic localizing instrument. *Radiology*, 1967, *89*, 329–331.
5. Todd, E. M. Manual of Stereotaxic Procedures. Privately published by Mechanical Developments Company, South Gate, California, 1967.
6. Waltz, J. M., and Cooper, I. S. Comparative study of ventriculography and pneumoencephalography for roentgenographic landmarks during cryothalamectomy. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1966, *97*, 583–587.

AN IMAGE ENLARGEMENT SCALE FOR STEREOTACTIC SURGERY*

By EDWIN M. TODD, M.D.,† *and* BENJAMIN L. CRUE, JR., M.D.†
SAN MARINO, CALIFORNIA

IN THIS day of wondrous achievements in communication systems, a curious contrast exists in the language of stereotactic statistics. We speak eloquently of precision techniques and sophisticated equipment, but a meaningful exchange in terms of precise measurements is obviated by the lack of common standards for adjusting

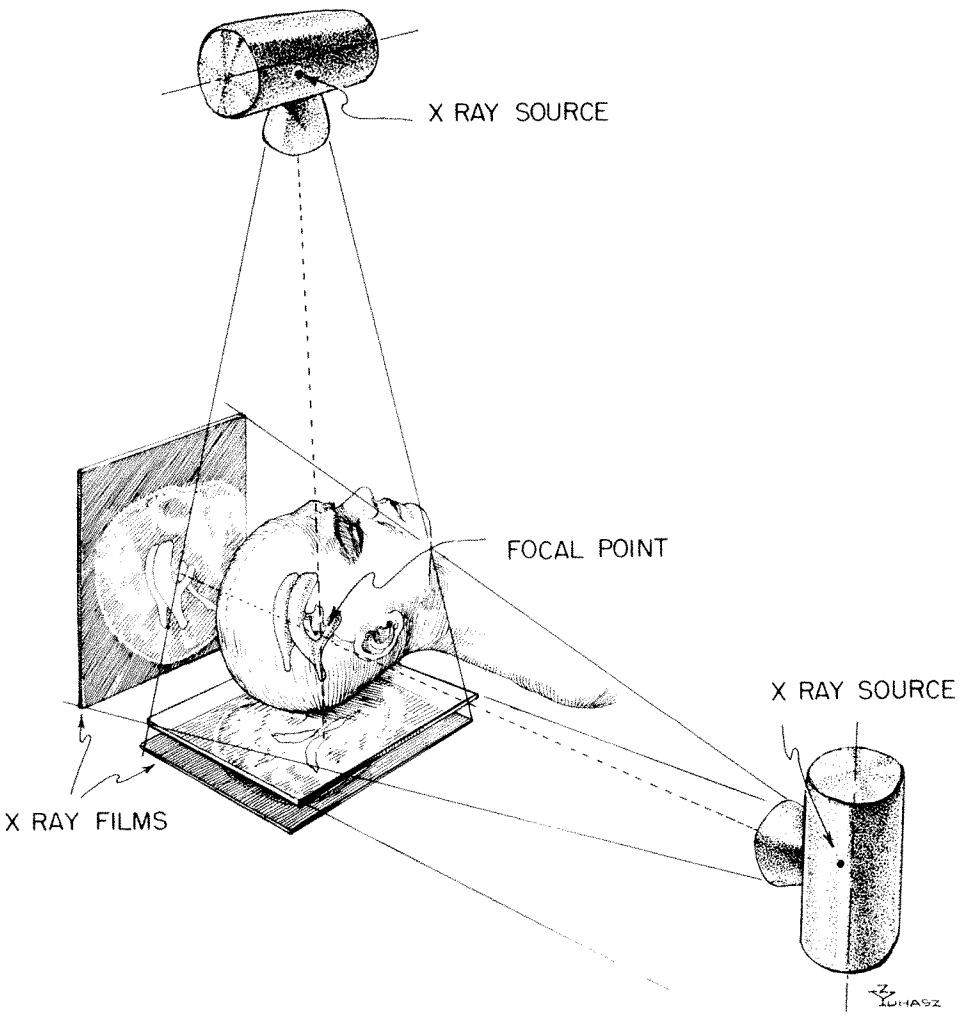


FIG. 1. Diagrammatic representation of the head positioned for surgery as it would appear in a stereotactic unit. In this particular instrument, the focal point is a constant fixture in relationship to the anteroposterior and lateral film placements. The head moves in 3 planes to bring the target to the focal point where x-ray emissions cross.

* From the San Marino Neurological Center, San Marino, California and the Department of Surgery, University of Southern California, Los Angeles, California.
† Associate Clinical Professor of Surgery (Neurological), University of Southern California, School of Medicine.

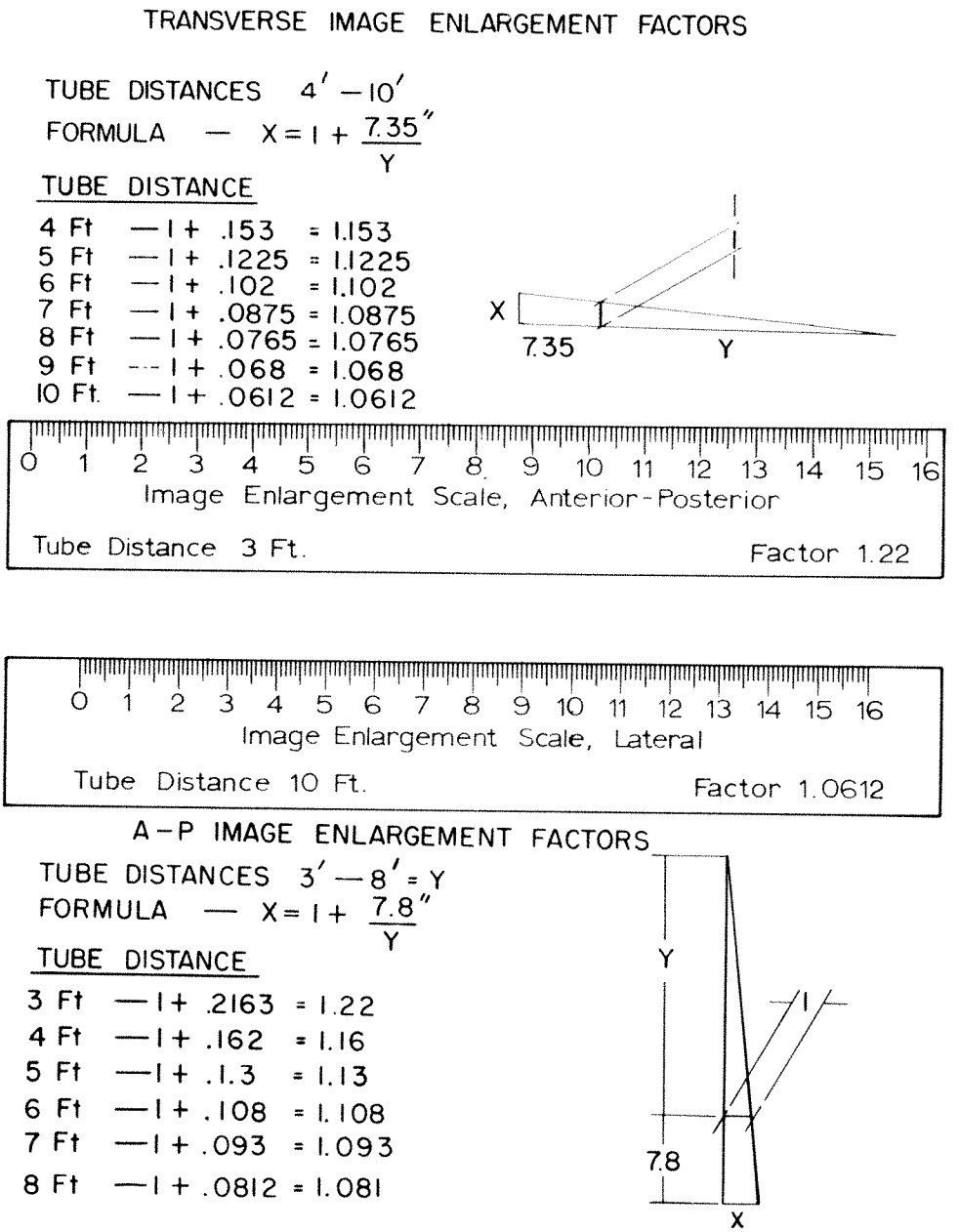


FIG. 2. Image enlargement scales were made by roentgenographing a radiopaque centimeter scale with zero at the focal point for each projection. Y designates the various tube distances for which scales were made. These image enlargement scales were randomly selected as examples for each projection with computation of enlargement factors for a complete set.

image distortions. Where spacious operating room facilities allow distant placement of x-ray equipment for all projections, correction figures may be negligible, but in crowded quarters, image enlargement is rather significant. Comparative statistics become meaningless. This failure to designate image enlargement factors discredits most of the charts used for diagramming skull and ventricle dimensions. It is a formidable obstruction to cumulative analysis in stereotactic surgery. An *image correc-*

tion scale is proposed as a means of establishing a universal reference standard.

MATERIAL AND METHOD

Figure 1 illustrates the design from which a set of scales was made for a specific instrument, the Todd-Wells Stereotactic Guide, a unit which orients the focal point with the target area. Whereas this does imply a limited application, designation of an enlargement factor for each scale allows for broader usage if the ratios are maintained. In Figure 2 derivation formulae are included for a complete set of scales in both projections. Distances from focal point to film are constants which may not be applicable to other stereotactic units; however, this can be resolved by compensatory adjustment of distance from focal point to x-ray source to preserve the integrity of the enlargement factor.

CONCLUSIONS AND SUMMARY

A set of scales is presented for the purpose of drawing attention to the urgent need for stereotactic statistics that are translatable in common terms. These scales are designed to convert multiple combinations of tube and film distances to infinity readings, and thereby establish a reliable frame of reference for accurate Atlas measurements.

Edwin M. Todd, M.D.
San Marino Neurological Center
2233 Huntington Drive
San Marino, California 91108

The authors gratefully acknowledge the invaluable assistance rendered by the following associates in the preparation of this work: Mr. Trent Wells of Mechanical Developments Company, South Gate, California, Engineer; Mr. Zolton Yuhasz, Medical Illustrator; John Camp, Jr., M.D., Radiologist; and Mr. James Whitson, R.T.

VOL. 105, NO. 2

STEREOTAXIC TRANSSPHENOIDAL BIOPSY AND CRYOSURGERY OF PITUITARY TUMORS*

By ROBERT W. RAND, PH.D., M.D., GUNNAR HEUSER, PH.D., M.D., ALFRED DASHE, M.D., DONALD ADAMS, M.D., *and* NATHAN ROTH, M.D.
LOS ANGELES, CALIFORNIA

PITUITARY adenomas can be classified clinically into non-secretory or secretory neoplasms. The vast number of tumors classified pathologically as chromophobe adenomas is included in the nonsecretory group. These neoplasms cause varying degrees of hypopituitarism due to compression-destruction of the residual pituitary gland. The clinical manifestations generally commence with gonadotropic dysfunction followed by thyrotropic and melanotropic failure and finally progressive decrease of ACTH-adrenal function. In addition, optic nerve and/or optic chiasm compression, and occasionally cavernous sinus syndromes involving the extraocular nerves, develop secondary to extrasellar extension in the appropriate direction.

The secretory pituitary tumors (classified pathologically as eosinophilic, basophilic, or mixed eosinophilic-chromophobe adenomas) produce such endocrine disorders as acromegaly, Cushing's disease, Nelson's hyperpigmentation syndrome,[17] and Chiari-Frommel's syndrome. These clinical entities depend upon the particular pattern of abnormal production of pituitary hormones; *i.e.*, excessive growth hormone, ACTH, MSH and lactogenic hormones, respectively.

In years past most endocrinologists, radiologists and neurosurgeons have accepted an enlarged "ballooned" sella turcica, a syndrome of hypopituitarism and, if present, bitemporal hemianopsia as the *sine qua non* for a clinical diagnosis of a pituitary tumor. This conclusion has been reached without much consideration about establishing a definitive histopathologic diagnosis. Consequently, hundreds, if not thousands, of patients in the world with "presumed chromophobe adenomas" have been treated by the radiotherapist without his having a pathologic tissue diagnosis.

The syndrome of an enlarged sella turcica and hypopituitarism with or without bitemporal hemianopsia may not be due to a radiosensitive chromophobe adenoma, but rather to one of the following pathologic entities which has no particular response to radiation or, at best, a very minimal response: for example, a carotid artery aneurysm, craniopharyngioma, meningioma, chordoma, cystic pituitary adenoma or especially sella turcica enlargement secondary to dilatation of the anterior third ventricle protruding into the sella turcica as a result of some slow progressive form of hydrocephalus, *e.g.*, progressive benign aqueduct stenosis.

The lack of exact histopathologic diagnosis is of further significance, when one considers the potential ill effects, both acute and delayed, of external radiation delivered to an enlarged sella turcica and the immediately surrounding brain structures including the hypothalamus, optic chiasm and nerves, the extraocular nerves and the mesial aspects of the temporal lobes.[6,7,18,25]

Therefore, we have taken the position, over the past several years, that a serious attempt should be made to establish a pathologic diagnosis by stereotaxic needle biopsy in presumed intrasellar neoplasms before employing external radiation therapy. Prior to such a surgical diagnostic procedure, each patient must have a careful and complete neuro-ophthalmologic, neuroendocrine, neurosurgical and neuroradio-

* Presented at the Fiftieth Annual Meeting of the American Radium Society, Miami Beach, Florida, April 7–11, 1968.
From the Departments of Surgery and Medicine, University of California, Los Angeles, School of Medicine, Los Angeles, California, and the UCLA Neuroendocrine Research Clinic.

logic work-up. Internal carotid angiography should be performed to rule out intracranial aneurysms which might be simulating a nonsecretory pituitary tumor. The exact position of the anterior cerebral arteries and the cavernous sinus carotid arteries will also throw light on the presence or absence of an extrasellar extension superiorly and/or laterally.

Pneumoencephalography with laminagraphy gives considerably more information than routine pneumoencephalographic views. This technique is done at UCLA Hospital using the Mimer universal head unit. The study is multipurpose. It supplements plain roentgenographic and laminagraphic studies of the sella turcica, and can accurately outline the extent and direction of suprasellar tumor growth. In addition, the position of the optic chiasm over the pituitary tumor can usually be determined by careful roentgenographic studies of the anterior floor of the third ventricle. This is of significance to the neurosurgeon in planning the appropriate surgical approach; that is, transfrontal, transfrontal-transsphenoidal or transsphenoidal operation,[20] and to some extent to the radiotherapist in determining the position and size of external portals for radiation therapy. Laminagraphic pneumoencephalography will demonstrate the position and extent of intrasellar air. Therefore, the shape and size of any intrasellar mass can be determined, if the sella is enlarged out of proportion to the intrasellar contents. If the subarachnoid space extends along the anterior wall of the sella turcica, stereotaxic procedures may be contraindicated for fear of producing a serious cerebrospinal rhinorrhea.

The use of these two neuroradiologic modalities (carotid angiography and pneumoencephalography with laminagraphy) in the diagnosis of pituitary tumors immediately raises the question of risk. To the current authors, the risk, including a general anesthetic if necessary, is reasonable in exchange for the information obtained. The risk can be lessened by having the patient with hypopituitarism in endocrine balance, particularly by giving supplementary cortisone therapy. This therapy lessens the incidence of hypotensive episodes due to borderline adrenal function during the performance of pneumoencephalography and appears to sustain the blood-brain barrier from passage of the contrast material during cerebral angiography.

A number of questions regarding stereotaxic transsphenoidal needle biopsy of pituitary tumors are immediately raised when this procedure has been recommended to a radiotherapist. For example, the risk of cerebrospinal rhinorrhea and meningitis, pituitary hemorrhage (apoplexy), accuracy of pathologic diagnosis and so forth. These questions are best answered by briefly describing the techniques involved.

TECHNIQUE

The surgical principles of stereotaxic cryohypophysectomy and pituitary tumor biopsy are essentially the same with some modifications. In preparation for either procedure, the patient receives a daily pHisoHex shampoo and cleansing of the nasal passages with ¼ per cent neo-synephrine nose drops followed by an antibiotic solution (usually bacitracin, 500 units per cc.) to reduce the chances of scalp and sinus infections, respectively.

If cryogenic lesions are to be produced, the patient is intubated awake under topical anesthesia and then anesthetized with fluothane in a manner to allow the patient to be awakened, but kept in a state of amnestic analgesia when the cryogenic lesions are made (Fig. 1). The patient is given intravenous demerol and Vistaril to accomplish this anesthetic state. In this manner, even though incipient ocular or extraocular motor nerve palsies may develop (10 per cent of cases), they will disappear with discontinuance of the flow of liquid nitrogen in the cryoprobe. This is an important safety feature of cryohypophysectomy compared to other techniques, such as, radiofrequency heat, or implanta-

tion of radioactive gold 198 or yttrium 90. It has been known for many years that nerve function will cease between temperatures of +1°C. and +15°C. Return to normal function will occur when the nerve is warmed to the body temperature. Since the inception of cryohypophysectomy in 1963, we have not had a single instance of permanent ocular or extraocular motor nerve palsy in over 100 cases.

The Rand-Urban stereotaxic instrument provides accuracy to 0.5 mm. and the arc assembly can be adjusted to place the center of the pituitary tumor in the center-point of the radii of the double-arc system (Fig. 2). The twist-drill guides inserted through the nose will permit a twist-drill hole to be placed in the anterior wall of the sella turcica and through the capsule of the tumor. In general, a 2.5 mm. hole will suffice to permit the insertion of a thin-walled long biopsy needle into the center of the presumed pituitary tumor (Fig. 3). Syringe suction on the needle will determine if the tumor is cystic or solid, and allow the surgeon to obtain tumor tissue for pathologic diagnosis, using either frozen and/or permanent histologic sections. The tissue obtained is made into a tissue button by a centrifuge in order to prepare serial sections (Fig. 4). In general, we have made permanent histopathologic sections using hematoxylin and eosin stain. Other tissue stains may be required to establish an accurate pathologic diagnosis.

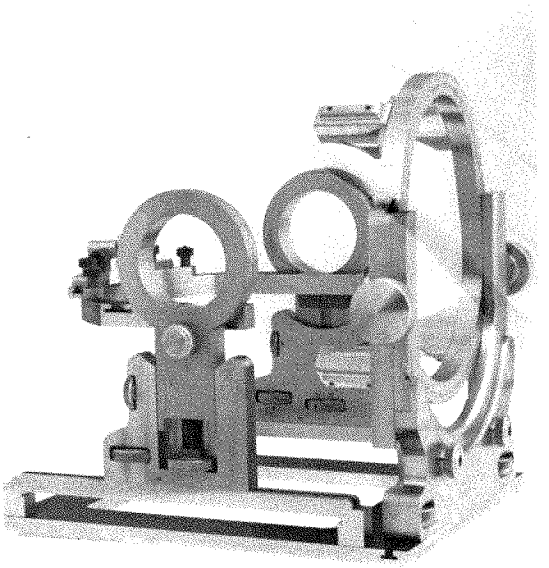


Fig. 2. Rand-Urban stereotaxic instrument is accurate to 0.5 mm., and provides independent vertical, rotatory, and horizontal movements of the head holder and the arc systems.



Fig. 1. Photograph of patient undergoing stereotaxic cryohypophysectomy. Note cryoprobe passing into right nostril. Patient is conscious with amnestic analgesia anesthesia in order to be able to test functions of CN II, III, IV, and VI, and thereby avoid permanent nerve palsies.

If insufficient neoplastic tissue is obtained, a larger twist-drill hole (3.2 mm.) is made and a larger diameter needle is reinserted into the tumor. If this fails to give an adequate amount of tumor tissue, then the procedure is either discontinued or a special Urban rotodissector instrument is inserted into the tumor. By using gradually increasing degrees of suction, neoplastic tissue is drawn into the side hole of the outer tube and cut off by the rotating inner blade powered by a small electric engine.

The 2.5 mm. twist-drill hole will heal by



FIG. 3. Lateral roentgenogram of transsphenoidal stereotaxic needle biopsy of pituitary tumor under general anesthesia after partial pneumoencephalography.

granulation tissue in a few days to be covered eventually by normal mucous membrane. Larger twist-drill holes (3.2 mm.) should be sealed to prevent cerebrospinal rhinorrhea. We insert a sterile cylinder of fine white silicone sponge marked for roentgenographic purposes by a central stainless steel wire. In this manner, its exact position in relation to the drill hole can be determined by fluoroscopy or roentgenography. Cerebrospinal rhinorrhea or meningitis with only stereotaxic biopsy of tumors has not occurred. If there has been any evidence of bleeding through the biopsy needle, a small piece of gel-foam soaked in thrombin, or a small piece of Surgicel is passed into the site from which the biopsy has been taken. It is possible to treat apoplexy of a pituitary tumor by transsphenoidal stereotaxic needle drainage of the hemorrhage in order to tide the patient over the acute symptoms of severe headache and subarachnoid hemorrhage which are due to the sudden hemorrhagic swelling and enlargement of the tumor.

RESULTS

An accurate pathologic diagnosis has been established in 90 per cent of the presumed pituitary tumors by using this needle biopsy technique. This series includes 35 pituitary tumors treated by cryohypophysectomy and 12 pituitary adenomas subsequently treated by external irradiation only. Up to the present time, we have had 2 patients who did not harbor pituitary tumors. One had some unusual type of parasellar mucoid cyst causing extraocular nerve palsies which disappeared with simple drainage. The other patient had a malignancy in the sphenoid sinus which was subsequently irradiated.

Stereotaxic cryohypophysectomy has been used to treat metastatic mammary and prostate carcinoma, progressive diabetic retinopathy, and secretory pituitary tumors with the clinical syndromes of acromegaly, Cushing's disease and Nelson's hyperpigmentation syndrome.[4,19,20,22] In a few instances, it has been employed as a primary (2) or secondary (4) treatment of chromophobe adenomas. The following discussion will be concerned with the category of secretory pituitary tumors causing acromegaly.

DISCUSSION

As was recently pointed out by Adams and his associates,[1] acromegaly is a disease that can lead to either disability or death from hypermetabolism (ultimately causing cardiac failure), diabetes mellitus with its known complications, and, in rare instances, intracranial extension of the tumor. Therefore, early effective treatment should be the ultimate goal and is dependent on early diagnosis. To this end Berson and Yalow and their associates[2,5] and others[10] have developed accurate radioimmunoassay of growth hormone (somatotropic hormone) which will determine the normal and abnormal serum levels in any given individual under circumstances of

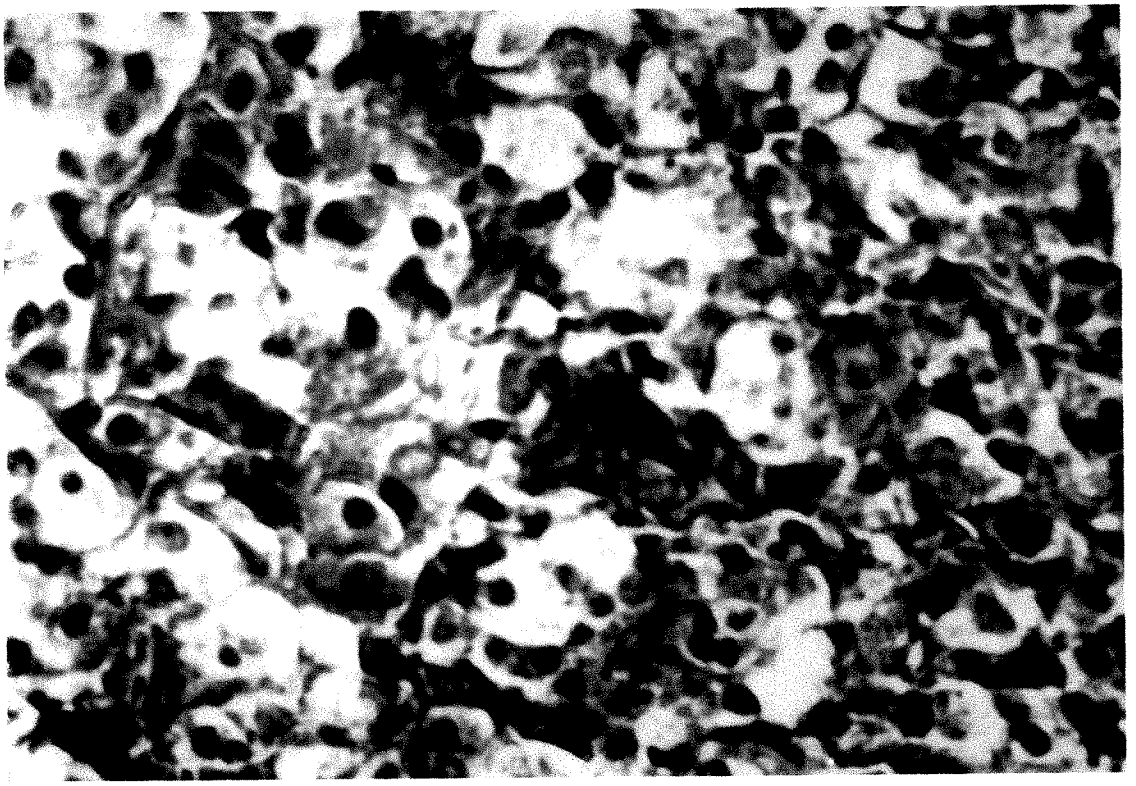


Fig. 4. Photomicrograph of stereotaxic needle biopsy specimen of eosinophilic adenoma just prior to cryohypophysectomy.

fast and glucose tolerance. Therefore, the relative biologic activity of a particular pituitary adenoma, insofar as growth hormone is concerned, can be estimated and compared to the historical events of acromegaly in the individual patient. The clinical effectiveness of a particular method of treatment can be compared with this laboratory technique.[12,15,16] Moderate clinical improvement has been associated with decrease, but not necessarily return to normal levels, of growth hormone. In one instance, a second cryohypophysectomy was performed and further improvement of the acromegalic features with a concomitant drop in serum growth hormone level was accomplished.

No method of treatment is invariably or totally effective and each procedure has its hazards. We are certainly not opposed to craniotomy[24] as a means of therapy for acromegaly, but feel that it is most applicable to the patient with an extensive lobulated tumor and those with extrasellar extension causing cranial nerve compression (CN II, III, IV, VI). Under these circumstances, craniotomy is relatively acceptable to the patient and his personal physician.

Transsphenoidal implantation of radioactive gold 198 and/or yttrium 90 has been associated with extraocular and optic nerve palsies as well as cerebrospinal rhinorrhea and meningitis.[9,11] Generally, the results have been more variable than those of cryohypophysectomy.

The most effective form of external irradiation of pituitary tumors causing acromegaly has been heavy particle irradiation.[13,14,16] This technique has the hazard of damage to adjacent brain structures, delay in obtaining the final clinical result (up to 3 years), relative unavailability of the radiation source for clinical use and the fact that patients previously treated by more conventional external



FIG. 5. Basal view of cavernous sinus venogram of pituitary tumor growing slightly asymmetrically.

irradiation cannot be treated safely by secondary heavy particle irradiation.

In order to increase the effectiveness of cryohypophysectomy, which we still consider to be under development, the technique of cavernous sinus venograms was evolved.[8,23] This study is performed by either a retrograde injection of the internal jugular veins or the frontal vein. It will accurately demonstrate the extent and direction of lateral growth of the intrasellar tumor and whether or not the cavernous sinus has been invaded or compressed by the tumor (Fig. 5). It has been a frequent observation that intrasellar pituitary tumors, in contrast to those which extend superiorly through or above the diaphragma sellae, tend to grow asymmetrically. When the results of the cavernous sinus venography are correlated with the other neuroradiologic data (plain roentgenographic and laminagraphic studies, pneumoencephalography and carotid angiography), a reasonably accurate model of the geometry of the particular pituitary tumor can be constructed. This information has led to improved positioning of the cryoprobes within the pituitary tumor to produce the appropriate cryogenic lesions for tissue destruction (Fig. 6). For example, if the pituitary tumor extends 14 mm. to the left of the midline, the cryoprobe is positioned in the geometric center of this lateral extension.

The extent of tissue necrosis by cryosurgery is determined by the heat generated in the tissue, and the time and temperature of cryogenic exposure. If a tissue, for example, the pituitary gland, which has a rich blood supply and is surrounded by large vascular structures such as the cavernous sinuses and the internal carotid arteries, is to be completely destroyed, the tip temperature of the cryoprobe must be between −180°C. and −184°C. The minimal time of cryogenic exposure for adequate destruction is 5 minutes, after which equilibrium in the tissue is more or less established (Fig. 7). Initially, a needle thermocouple was inserted through the opposite nasal passage into the pituitary gland or tumor and it was found, for example, that at about 7 mm. from the cryoprobe, the tissue temperature was greater than −12°C. Generally a tissue temperature of −20°C. is required

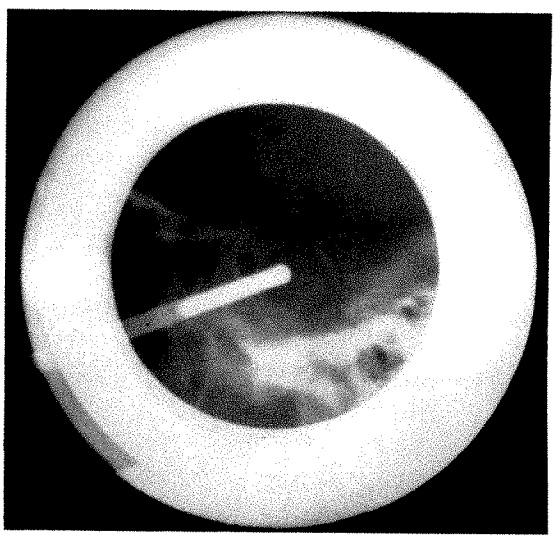


FIG. 6. Lateral roentgenogram showing Linde cryoprobe placed stereotaxically in an eosinophilic adenoma of an acromegalic patient for 1 of 3 cryogenic lesions (−184°C. × 10 inches).

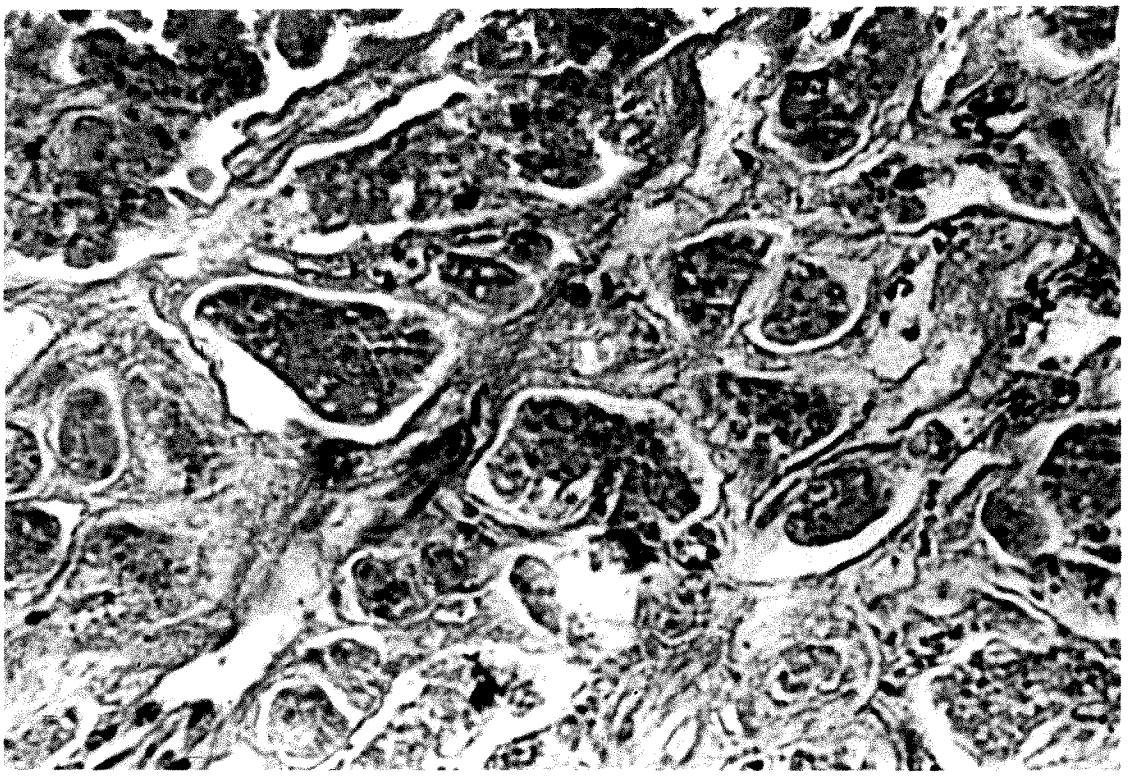


Fig. 7. Photomicrograph of pituitary gland showing characteristic coagulation necrosis of cryohypophysectomy.

to be certain of tissue necrosis within the ice-ball formation about the cryoprobe. Destruction of the anterior lobe of the normal pituitary gland can usually be accomplished by two overlapping cryogenic lesions 4 mm. on either side of the midline with the small cryoprobe (2.74 mm. in diameter). The cryoprobe should not extend behind the geometric center of the sella turcica. Using this configuration the patient rarely has had any significant diabetes insipidus, and yet adrenal, thyroid and gonadal function tests will indicate total ablation of production of these hormones.

In the case of a pituitary tumor with a slightly enlarged sella turcica, the small cryoprobe (2.74 mm. in diameter) is employed, while larger (3.2 and 4.76 mm. diameter) cryoprobes are used for moderate and large intrasellar tumors. The number of cryogenic lesions required varies from 2 to 4 on each side depending upon the size of the tumor and the size of the cryoprobe employed. As pointed out earlier, when the larger sized cryoprobes are used, the twist-drill holes must be sealed in order to prevent cerebrospinal rhinorrhea. Five patients have developed this complication as a result of inadequate sealing of the twist-drill holes and in 3 patients meningitis occurred. This complication led to the death of 2 of these patients (Fig. 8). The second patient developed meningitis following a second stage left-sided cryohypophysectomy 1 week after the right side of the tumor had been destroyed. In addition, this patient had bleeding from the cavernous sinus when the twist-drill was deflected laterally by heavy bone development in the floor of the sella turcica. Since that time, the twist-drill system has been modified by strengthening and lengthening the drill guides. There has been no further instance of deflection of the drill with these innovations. The third patient



FIG. 8. Sagittal section of autopsy specimen (Case 12, Table II) of decalcified eosinophilic adenoma. Microscopic studies showed complete necrosis of the adenoma with partial preservation of residual pituitary gland in posterior superior area of the enlarged sella turcica.

recovered with appropriate antibiotic therapy.

Under construction are specially designed cryoprobes which will allow a fine needle containing a thermocouple system to be passed along the side of the cryoprobe and advanced to a known distance ahead of the tip of the cryoprobe. The distance from the probe can be varied from 1 mm. to 10 mm. Therefore, the exact tissue temperature at a particular point can be determined in each tumor and at each site of the cryoprobe placement. In this manner an accurate geometric three dimensional design of the overlapping cryogenic lesions can be made and correlated with the geometric construction of the pituitary tumor obtained from the neuroradiologic studies.

It is of some interest that 2 patients who have shown dramatic improvement of their acromegalic syndrome (1 with partial bitemporal hemianopsia) have had the pneumoencephalogram repeated 2 years after the cryogenic surgery. In the first patient, this was done because she developed retrobulbar optic neuritis which was effectively treated by temporarily increasing the cortisone therapy for a period of time. It was felt that the optic neuritis was not related to the acromegaly or the original pituitary tumor. However, in order to rule out compression of the optic chiasm or nerves, pneumoencephalography with laminagraphy was repeated. The diaphragma sellae was sunken into the still enlarged, but recalcified sella turcica as compared to the bulging diaphragm that was present before. In the second patient a similar study was done because of severe headaches of unexplained origin. This particular patient also showed the same deep intrasellar depression of the diaphragma sellae as compared to a previous mild suprasellar extension of the pituitary tumor which had caused the partial optic chiasm compression (Fig. 9, *A* and *B*). This particular patient had regression of the bitemporal hemianopsia and return of visual acuity to normal within 3 weeks after the cryohypophysectomy.

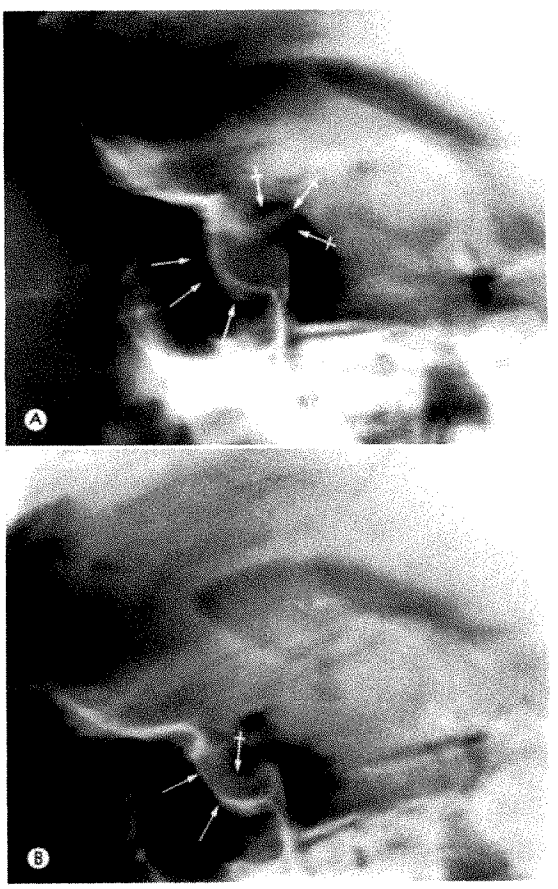


FIG. 9. (*A*) Pneumoencephalogram immediately before cryohypophysectomy shows suprasellar extension of eosinophilic tumor in an acromegalic patient with partial bitemporal superior quadranopsia. (*B*) Similar study 2 years after cryosurgery with inversion of diaphragma sellae into the recalcified, but still enlarged, sella turcica.

A few comments should be made about our experience with patients who have had stereotaxic cryohypophysectomy for known chromophobe adenomas. One young lady who had had a craniotomy elsewhere for suprasellar extension of her chromophobe adenoma causing bitemporal hemianopsia developed recurrence of visual symptoms within 6 months. This was partially improved by external irradiation using cobalt 60 (4,000 r tumor dose). Six months later, or 1 year after the initial craniotomy, the chiasmatic syndrome recurred. This time, because of a *Staphylococcus* scalp and bone infection, the cryohypophysectomy was performed. Complete remission of the bitemporal hemianopsia occurred. The patient remained in remission for 3 years and then had her third recurrence of visual loss. A second stereotaxic procedure was carried out uneventfully and she is now again in remission of her clinical syndrome. Cryohypophysectomy has been of palliative benefit to this patient when both craniotomy and external irradiation failed.

A second patient who had had 2 previous craniotomies elsewhere for chromophobe adenoma had an attempt at the stereotaxic cryohypophysectomy. He developed temporary amaurosis of the left eye with one cryogenic lesion. The vision in this eye was 20/200 before surgery and returned to 20/30 three weeks after surgery. A third craniotomy was done at UCLA Hospital to remove the tumor that lay behind the optic chiasm. The intrasellar tumor was necrosed on the left side; the remainder was removed with microneurosurgical techniques. A third patient showing the same general problem with possible malignant chromophobe adenoma had extensive cryosurgical lesions made in the intrasellar portion of the tumor. At the third craniotomy several months after the cryohypophysectomy, there was no viable tumor in the intrasellar space. Tumor remained about the right optic nerve and behind the optic chiasm and was removed.

Therefore, cryohypophysectomy is probably not indicated in most cases of chromophobe adenoma where the tumor can be clearly demonstrated to pass 1 cm. or more above the level of the diaphragma sellae. On the other hand, if the tumor is confined within the sella, and, particularly, if it is cystic and, therefore, less responsive to external irradiation, cryosurgery may be of value. Experience with this particular problem has been limited to 2 cases with inadequate time to report follow-up.

Table 1 summarizes 16 patients with acromegaly initially treated by some type of external irradiation. Conventional high voltage roentgen therapy did not result in subjective or objective improvement (Cases 2, 3, 4, 6, 10 and 16). The range of estimated tumor dose was between 605 r in Case 4 to 3,000 r in Case 2. One of these patients (Case 10) had 2,500 r by a conventional source and 4,000 r by cobalt 60 10 years later without altering the progression of the acromegaly.

Eight patients (Cases 1, 7, 9, 10, 12, 13, 14 and 15) received cobalt 60 therapy with a tumor dose range between 1,000 r (first course of Case 1) to 5,500 r in Case 14. Six of these 8 patients had 4,000 r tumor dose or more. Five patients had no evidence of clinical remission while 3 had some temporary lessening of the soft tissue growth associated with the acromegaly; in these 3 patients their physicians observed recurrence of soft tissue growth.

Three patients were treated by a linear accelerator (Linac), each receiving slightly more than 5,000 r tumor dose. Temporary remission was observed by the endocrinologists in 2 and no response in 1. The pretreatment growth hormone immunoassay declined in 2 of these patients (Cases 8 and 11), but still remained abnormally elevated in Case 11.

It seems appropriate to point out that the observations as to results after external irradiation were made by others than the current authors.

Table 11 outlines the clinical course of the same 16 patients shown in Table 1 after cryohypophysectomy. In these patients growth hormone immunoassay (Fig. 10)

TABLE I

SUMMARY OF 16 PATIENTS WITH ACROMEGALY INITIALLY TREATED BY SOME TYPE OF EXTERNAL IRRADIATION

Patient	Radiation Therapy Tumor Dose			Growth Hormone Assay G.T.T. Control/Low		Results
	Cobalt 60	Conventional	Linac	Pre-treatment	Post-treatment	
1. M. B.	1,000 r—2/61 2,400 r—2/63	—	—	—	—	T→R
2. K. A.	—	3,000 r—1960	—	—	—	O
3. R. E.	—	3,024 r—1959 2,379 r—1962	—	—	—	O
4. M. D. Q.	—	605 r—8/63 1,620 r—11/63 1,300 r—7/64	—	—	—	O
5. E. M.	—	—	5,145 r—1964	—	—	O
6. L. B.		2,970 r—1953 2,000 r—1957		—	—	O
7. G. D.[1]	4,000 r—1964	—	—	—	—	O
8. R. C.	—	—	5,085 —1964	15/12	9.1/6.4	T→R
9. M. P.	4,100 r—9/63			—	—	T→R
10. G. D.[2]	4,000 r—1964	2,500 r—1954	—	—	—	O
11. N. A.	—	—	5,184 r—1963	44	29	T→R
12. A. D.	4,000 r—1964	—	—	—	—	O
13. L. W.	4,665 r—1962	—	—	—	—	O
14. W. W.	5,500 r—1964	—	—	—	—	O
15. J. R.	2,597 r—1965	—	—	—	—	T→R
16. A. M.		1,800 r—1956		—	—	T→R

T = transient improvement.
R = recurrent syndrome.
O = no response.
1 and 2 = same patient.

before and after treatment was available in 9 (Cases 1, 2, 3, 4, 5, 8, 9, 10 and 11). In 6 of these patients postoperative levels were normal or below normal levels (Cases 1, 3, 4, 5, 8 and 9), and in each of these instances the patients have shown dramatic and continued remission as demonstrated in Figure 11, *A* and *B*.

In 1 patient the levels of growth hormone became borderline (Case 2) while in another it was slightly above normal. However, both of these patients have

Table II

CLINICAL COURSE OF SAME 16 PATIENTS SHOWN IN TABLE I AFTER CRYOHYPOPHYSECTOMY

Patient	Date of Cryohypophysectomy	Growth Hormone Assay G.T.T. Control/Low		Results Remission		Complications
		Pre-operative	Post-operative	Objective	Subjective	
1. M. B.	11/18/63	64	<2	+	+	—
2. K. A.	8/31/64 and 5/3/66	>40/>40	12/>10	+	+	—
3. R. E.	1/13/65	30/25	8.6/8.6	+	+	—
4. M. D. Q.	3/25/65	22/15	2.7/<2	+	+	—
5. E. M.	6/1/65	52/27	3.7/3.3	+	+	R, D.I., M
6. L. B.	7/23/65	NA	NA	o	o	R
7. G. D.[1]	7/23/65	NA	NA	+	+	—
8. R. C.	1/17/66	9.1/6.4	4.4/<4	+	+	—
9. M. P.	1/20/66	9.6/5.1	<2/<2	+	+	D. I.
10. G. D.[2]	3/28/66	23	18/12	+	+	—
11. N. A.	4/27/66	24/>32	>32/>32	o	o	—
12. A. D.	7/11/66	NA	NA	—	—	Expired 8/13/66 R, M
13. L. W.	8/30/66	4.7/5.0	NA/NA	+	+	—
14. W. W.	3/15/67	NA	NA	—	—	Expired 4/2/67 M, S
15. J. R.	8/4/67	NA	NA	+	+	—
16. A. M.	10/11/67	>32/>32	NA	+	+	—

R = cerebrospinal fluid rhinorrhea.
D.I. = diabetes insipidus.
M = meningitis.
S = stroke.
+ = remission.
O = no response.
1 and 2 = same patient.

shown moderate clinical improvement. In 1 patient the abnormal growth hormone levels remained essentially unchanged and as expected there was no clinical remission (Case 11).

Objective and subjective remission was observed in 4 additional patients (Cases 7, 13, 15 and 16) in whom growth hormone studies were either not available or were incomplete.

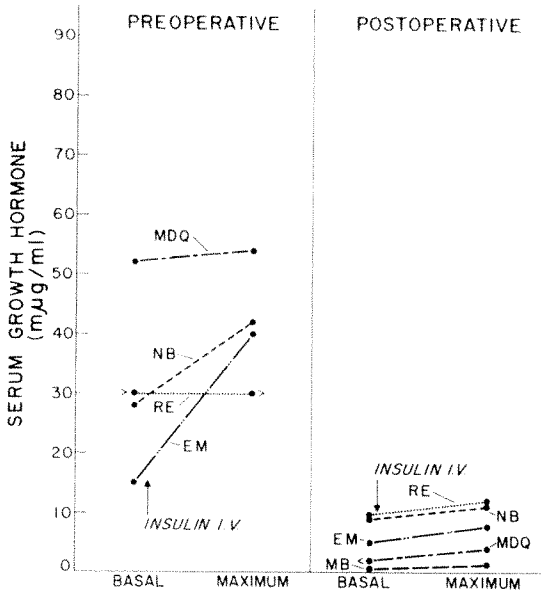


FIG. 10. Graph of pre- and posteryohypophysectomy serum growth hormone levels at basal and maximum response to intravenous insulin (Case 1, 3, 4 and 5, Table II); additional Case M. B. of reduced postoperative growth hormone levels.

These encouraging clinical results by cryohypophysectomy are not without morbidity and mortality. Two patients previously discussed died from complications of cerebrospinal rhinorrhea, meningitis and massive gastric hemorrhage in one, and meningitis and massive stroke in the other. Both patients had had advanced acromegaly with serious diabetes mellitus and hypertension. In the authors' opinion



FIG. 11. (*A* and *B*) Photographs of patient (Case 1, Table II). (*A*) Before and (*B*) 6 weeks after cryohypophysectomy for acromegaly. The striking remission continues to the present time.

these deaths could probably be avoided now by improved systems of twist-drill guides and of sealing the drill holes. One patient (Case 5) had cerebrospinal rhinorrhea and meningitis, but recovered after the leak was sealed stereotaxically. He has returned to his usual occupation.

Diabetes insipidus has required continued treatment in 2 of 30 patients who have undergone cryohypophysectomy. It is interesting that 1 patient only requires pitressin every 3 weeks, 3 years after surgery. He had required it every 2 days for several months immediately after operation. The other patient is on small doses of pitressin.

Not shown in Table II are the 14 remaining patients making up our total experience with acromegaly. Most of these have also shown striking or moderate improvement of their acromegaly. In this group there have been no serious complications or deaths. It is of some interest that the pituitary-adrenal axis can often be preserved by this cryogenic technique and yet obtain a striking remission of the acromegaly. Adams *et al.*[1] reported 13 of 16 patients who did not require steroid maintenance. In our series this number has not been quite as high.

CONCLUSION

Stereotaxic transsphenoidal cryohypophysectomy, particularly with improved measurements of cryogenic lesion size by modified cryoprobe, and complete neuroradiologic studies to construct the geometry of the tumor offers selected patients with acromegaly a reasonably safe and effective means of treatment when compared to the greater risks associated with craniotomy on the one hand, and the less impressive results, at least in our experience, of external irradiation, excluding heavy particle radiation therapy of which we have no personal experience.

In addition, stereotaxic transsphenoidal needle biopsy of presumed pituitary tumors is desirable before external irradiation is given in order to try and establish a definitive histopathologic diagnosis and thereby gain insight as to possible radiation response of the tumor.

Robert W. Rand, M.D.
Department of Surgery
University of California, Los Angeles
School of Medicine
Los Angeles, California 90024

We would like to thank Josiah Brown, M.D., for data on growth hormone; G. Wilson, M.D., Division of Neuroradiology, for performance and interpretation of roentgenographic examinations; Mrs. Mary Parker, R.N., for assistance in organizing clinical data; and Mrs. Barbara King for preparation of the manuscript.

REFERENCES

1. Adams, J. E., Seymour, R. J., Earll, J. M., Tuck, M., Sparks, L. L., and Forsham, P. H. Transsphenoidal cryohypophysectomy in acromegaly; clinical and endocrinological evaluation. *J. Neurosurg.*, 1968, *28*, 100–104.
2. Berson, S. A., and Yalow, R. Personal communication.
3. Bleasel, K., and Lazarus, L. Cryogenic hypophysectomy. *Med. J. Australia*, 1965, *2*, 148–150.
4. Dashe, A. M., Solomon, D. H., Rand, R. W., Frasier, S. D., Brown, J., and Spears, I. Stereotaxic hypophyseal cryosurgery in acromegaly and other disorders. *J.A.M.A.*, 1966, *198*, 591–596.
5. Glick, S. M., Roth, J., Yalow, R. S., *et al.* Regulation of growth hormone secretion. *Recent Prog. Hormone Res.*, 1965, *21*, 241–283.
6. Goldberg, M. B., Sheline, G. E., and Malamud, N. Malignant intracranial neoplasms, following radiation therapy for acromegaly. *Radiology*, 1963, *80*, 465–470.
7. Greenhouse, A. H. Pituitary sarcoma; possible consequence of radiation. *J.A.M.A.*, 1964, *190*, 269–273.
8. Hanafee, W. N., Rosen, L. M., Weidner, W., and Wilson, G. H. Venography of cavernous sinus, orbital veins, and basal venous plexus. *Radiology*, 1965, *84*, 751–753.
9. Hartog, M., Doyle, F., Fraser, R., *et al.* Partial pituitary ablation with implants of gold-198 and yttrium-90 for acromegaly. *Brit. M. J.*, 1965, *2*, 396–398.
10. Hunter, W. M., and Greenwood, F. C. Radio-

immunoelectrophoretic assay for human growth hormone. *Biochem. J.*, 1964, *91*, 43–56.

11. KAUFMAN, B., PEARSON, O. H., SHEALY, C. N., CHERNAK, E. S., SAMANN, N., and STORAASLI, J. P. Transnasal-transsphenoidal yttrium-90 pituitary implantation in therapy of acromegaly. *Radiology*, 1966, *86*, 915–920.
12. KOZAK, G. P., VAGNUCCI, A. I., LAULER, D. P., and THORN, G. W. Acromegaly pre- and post-pituitary irradiation. *Metabolism*, 1966, *15*, 290–303.
13. LAWRENCE, J. H., TOBIAS, C. A., BORN, J. L., GOTTSCHALK, A., LINFOOT, J. A., and KLING, R. P. Alpha particle and proton beams in therapy. *J.A.M.A.*, 1963, *186*, 236–245.
14. LAWRENCE, J. W., TOBIAS, C. A., BORN, J. L., SANGALLI, F. R., CARLSON, R. A., and LINFOOT, J. H. Heavy particle therapy in acromegaly. *Acta radiol.*, 1962, *58*, 337–347.
15. LAZARUS, L., BLEASEL, K. F., CONNELLY, T. J., *et al.* Serum-growth-hormone in acromegaly; effect of cryogenic pituitary destruction. *Lancet*, 1966, *2*, 90–91.
16. LINFOOT, J. A., and GREENWOOD, F. C. Growth hormone in acromegaly: effect of heavy particle pituitary irradiation. *J Clin. Endocrinol.*, 1965, *25*, 1515–1518.
17. NELSON, D. H., MEAKIN, J. W., and THORN, G. W. ACTH-producing pituitary tumors following adrenalectomy for Cushing's syndrome. *Ann. Int. Med.*, 1960, *52*, 560–569.
18. PECK, F. C., JR., and MCGOVERN, E. R. Radiation necrosis of brain in acromegaly. *J. Neurosurg.*, 1966, *24*, 536–542.
19. RAND, R. W. Stereotactic transsphenoidal cryohypophysectomy. *Bull. Los Angeles Neurol. Soc.*, 1964, *29*, 40–48
20 RAND, R. W. Cryohypophysectomy in pituitary tumors with comments on radical pituitary tumor excision using microneurosurgical technique. Proc. III International Congress of Neurological Surgery, Copenhagen, August 23–28, 1965. *Excerpta Med.* (International Congress Series), 1965, *110*, 788–793.
21. RAND, R. W. Cryosurgery of pituitary in acromegaly: reduced growth hormone levels following hypophysectomy in 13 cases. *Ann. Surg.*, 1966, *164*, 587–592.
22. RAND, R. W., DASHE, A. M., PAGLIA, D. E., CONWAY, L. W., and SOLOMON, D. H. Stereotactic cryohypophysectomy. *J.A.M.A.*, 1964, *189*, 255–259.
23. RAND, R. W., and HANAFEE, W. N. Cavernous sinus venography and stereotaxic cryohypophysectomy. *J. Neurosurg.*, 1967, *26*, 521–526.
24 RAY, B. S., and HORWITH, M. Surgical treatment of acromegaly. *Clin. Neurosurg.*, 1964, *10*, 31–59.
25. WALTZ, T. A., and BROWNELL, B. Sarcoma: possible late result of effective radiation therapy for pituitary adenoma; report of two cases. *J. Neurosurg.*, 1966, *24*, 901–907.

LOCALIZATION OF THE CALCIFIED PINEAL BODY ON LATERAL ROENTGENOGRAMS*

By CAPTAIN RONALD P. PAWL, MC, USA,† *and* CAPTAIN ARTHUR K. WALTER, MC, USA‡
HONOLULU, HAWAII

SINCE the classic work of Vastine and Kinney,[7] published in 1927, there have been presented at intervals in the radiographic literature either modifications of the measurements of those authors or alternative methods to the localization of the pineal gland on the lateral roentgenogram of the skull. The purpose of these efforts has usually been either to improve the accuracy of such localization or to present a more simplified method than that posed by Vastine and Kinney.

The first modification was proposed by Dyke[1] who found that in his own series of cases, 14 per cent fell outside of the Vastine-Kinney normal range and that most of these were displaced anteriorly. Consequently, it was suggested that the normal range be moved forward 4 mm.[6] But, as Taveras and Wood[6] and Oon[5] pointed out, this then causes a significant number of normals to appear displaced posteriorly. Therefore, at the Neurological Institute in New York, a ruler, which combines the system of Vastine and Kinney and the suggested modification of Dyke, has been used. The limits of normal on this ruler range up to 17 mm., and Taveras and Wood note that variations of 2–3 mm. outside of this range are probably normal.[6] Therefore, the use of this method results in a range of pineal gland measurements varying 20 mm. in the anteroposterior dimension and 18 mm. in the superoinferior dimension. This range is considerable and the use of this method requires either the aforementioned specially made ruler or the use of tables and charts which are somewhat cumbersome.

Fray[2,3] proposed 2 separate methods of pineal gland localization. The first is a proportional method in which an elastic is constructed and can be placed upon the roentgenogram, stretching to meet predetermined points on the cranial vault, and the pineal falls, in normal cases, within a predetermined limit drawn on the elastic. Using this method, Fray noted an accuracy of 93 per cent in the anteroposterior dimension and 94 per cent in the superoinferior dimension. Although this method fulfills the needs of accuracy, it does require the presence of a specially pre-constructed device. Fray's second method is based on angles which are drawn on a previously constructed overlay and, although the author found excellent accuracy with this system, Oon,[5] in comparing this method to his own, found that Fray's angles gave poor results.

The latest technique by Oon, whose work presents an excellent review of the various methods used to localize the pineal gland on lateral roentgenograms, is a method which is both simple and does not require the use of overlays, pre-constructed devices or graphs and charts.[5] The method is based on the construction of a 5 cm. perpendicular from the midsellar point on a line drawn from the tuberculum sellae to the basion. In his series, Oon noted that 98 per cent of all normal pineal bodies fell within a range of 10 mm. from the end point of this line. The difficulties that

* From the Neurosurgery and Radiology Services, U. S. Army Tripler General Hospital, Honolulu, Hawaii.
† Present Address: Department of Neurology and Neurological Surgery, Neuropsychiatric Institute, University of Illinois, Chicago, Illinois.
‡ Present Address: Radiology Service, U.S. Army Tripler General Hospital, Honolulu, Hawaii.
This material has been received by the Office of the Surgeon General, Department of the Army, and there is no objection to its presentation and/or publication. This review does not imply any indorsement of the opinions advanced or any recommendation of such products as may be named.

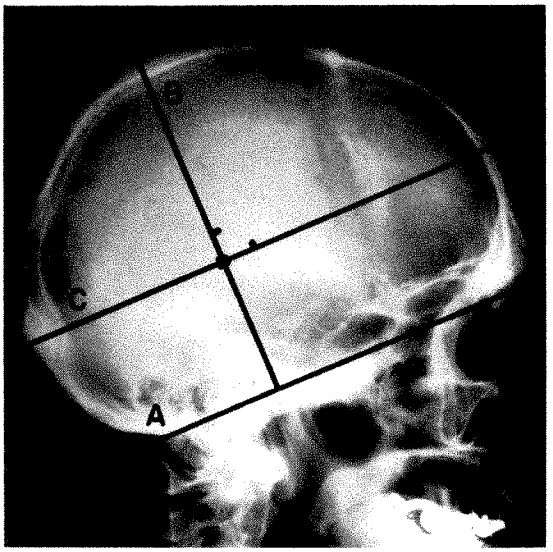


FIG. 1. Line A: The baseline from which all lines are constructed. Line B: Perpendicular to Line A. Line C: Parallel to Line A. Both intersect through the pineal body. Dots represent half-way points as described in text.

arise with this method are that a fixed focal distance is required, since the method does not account for proportional variation with different techniques, and the author also notes the need for perfect lateral roentgenograms. Thus, any movement of the head that might occur during the taking of routine skull roentgenograms would appear to make the technique unusable. In addition to the foregoing methods, there are others which have been described[4,5] which are either time-consuming or impractical in daily application.

METHOD

In an attempt to devise a method which meets the criteria of a high degree of accuracy, minimum range for normals, and the lack of required pre-constructed materials, overlays, graphs, or tables, we propose the following procedure of pineal body localization on lateral roentgenograms: A line is constructed along the base of the skull from the nasion to the lowermost portion of the basiocciput just posterior to the opisthion (Fig. 1, Line A). From this point, a perpendicular is drawn which passes through the center of the calcified pineal body (Fig. 1, Line B). A point is measured on the second line which is one-half the distance from the inner table of the cranial vault bone to the baseline; the pineal should lie 1 cm. below this point. A third line is then constructed which is parallel to the first line and perpendicular to the second line and runs through the calcified pineal body in its midportion (Fig. 1, Line C). A point on this line is measured half the distance from the inner table of the frontal bone to the outer table of the occipital bone and the pineal should lie 1 cm. posterior to this point.

We have used this method of localization on 120 cases of calcified pineal bodies over the last year at Tripler Army Medical Center. Although this group of patients represents primarily young adult military material, there is a significant number of retired military personnel in the area, and the high percentage of patients who are of Polynesian or Oriental background gives the series a variable cross-section of ages and races. The scattergram in Figure 2 shows the results of this method in localizing the pineal body. It is noteworthy that, as in the experience of previous authors, the

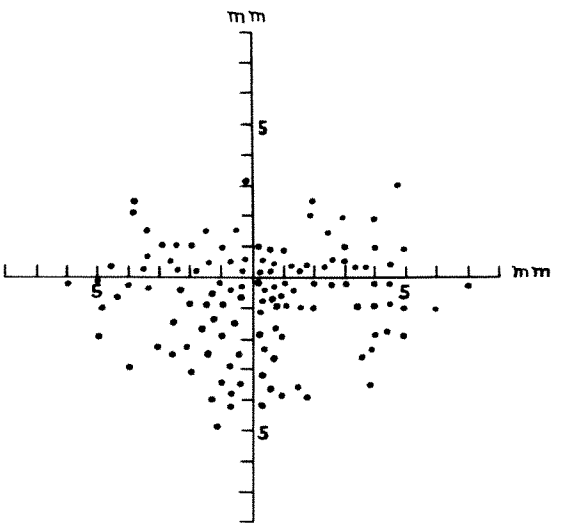


FIG. 2. Scattergram of 120 cases of calcified pineal bodies in normal patients demonstrating distribution using the authors' technique.

greatest accuracy of the method is in the superoinferior measurement in which 100 per cent of the cases were found to be within 5 mm. above or below the point. In the anteroposterior diameter, the accuracy is somewhat less, with only 98.5 per cent of cases being located within 5 mm. anterior or posterior to the expected normal point.

DISCUSSION

In Dyke's article reviewing the method of Vastine and Kinney,[1] the author analyzed 2,724 roentgenograms and found that 51 per cent of these had calcified pineal bodies. A slightly higher percentage was found in males than in females and, although under the age of 20, only 20 per cent of patients reviewed had roentgenographically visible calcification; over the age of 20, 55 per cent were visible. Consequently, it would seem worthwhile to attempt improvement of the methods for localization of this readily accessible structure on routine skull roentgenograms. The method we have described reduces the range of normal in our series to a square 1 cm. on each side. The location of this square is relative to the cranial vault itself and therefore not subject to variation because of variable roentgenographic technique. We have also found that moderate rotation or movement of the patient's skull during roentgen examination does not displace the calcified pineal body outside of this range of normal. The most accurate dimension of determination of the pineal body calcification using this method is in the superoinferior dimension, and all of the points measured fell within an 8 mm. range from a point 3 mm. above the measured spot to a point 5 mm. below it. And, although the anteroposterior dimension is less accurate, only 3 cases out of 120 fell outside of the 5 mm. range. It is significant to note in this respect that in Vastine and Kinney's[2] original article, all pineal bodies which were displaced in pathologic cases on the lateral roentgenograms were displaced in either a downward or downward and backward direction so that using the method we have just described, the dimension which is most significantly distorted in pathologic cases is the one which is most accurate in our series. Although this method would seem to require drawing lines on roentgenograms, in practice this has not been the case. By simply placing a straight edge in the appropriate positions and marking points on the roentgenograms which do not interfere with the interpretation of underlying bone structures, we have been able to successfully carry out these measurements with the accuracy noted above.

SUMMARY

1. A method of determining the normal position of the calcified pineal body on lateral roentgenograms is presented. This method does not require the use of preconstructed materials, devices, overlays, graphs or tables, although it does require the knowledge of a relatively simple rule.

2. The range of normal is reduced by this method in our series to 5 mm. above, below, in front of, or behind the calculated point, and the accuracy of this series in our hands was 100 per cent in the superoinferior dimension and 98.5 per cent in the anteroposterior dimension.

3. It is pointed out that the experience of previous authors has indicated the superoinferior dimension is the one most significantly affected in cases in which the pineal body is abnormally displaced, and this dimension in our series is the most accurate.

Captain Ronald P. Pawl, MC, USA
Department of Neurology and Neurological Surgery
Neuropsychiatric Institute
University of Illinois
912 South Wood Street
Chicago, Illinois 60612

REFERENCES

1. Dyke, C. G. Indirect signs of brain tumor as noted in routine roentgen examinations: displacement of pineal shadow. Am. J. Roentgenol. & Rad. Therapy, 1930, *23*, 598–606.
2. Fray, W. W. Roentgenologic study of orientation

VOL. 105, NO. 2

SUPRASELLAR SUBARACHNOID CYSTS*

RADIOCLINICAL FEATURES

By ANDRÉ SANSREGRET, M.D.,† ROGER LEDOUX, M.D.,† FERNAND DUPLANTIS, M.D.,‡ CHRISTIAN LAMOUREUX, M.D.,§ ALCIDE CHAPDELAINE, M.D.,‖ *and* PIERRE LEBLANC, M.D.¶

MONTREAL, QUEBEC, CANADA

AT the discovery of our first well documented suprasellar subarachnoid cyst, we were as much astonished by its precise radiologic delineation from the third ventricle as by its reduced clinical manifestation consisting of headaches precipitated by change of position.

We recently have seen a young female patient with another suprasellar subarachnoid cyst which was impossible to dissociate from the third ventricle. This cyst was associated with definite endocrinologic signs; namely, amenorrhea, relative nanism and retarded skeletal development. The emerging radioclinical signs in suprasellar subarachnoid cysts were therefore analyzed.

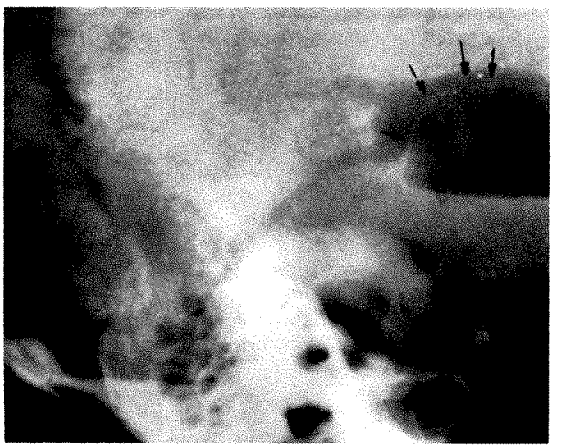


FIG. 1. *Suprasellar subarachnoid cyst of presumed cisternal origin.* Upright lateral position. There is fine delineation of the cyst from the floor of the third ventricle (arrows).

REPORT OF CASES

CASE I. A 45 year old patient was admitted with headaches of 6 months' duration. The patient complained of pain in the frontal area on leaning forward and coughing. The neurologic and ophthalmologic examinations were completely normal; there were no apparent clinical endocrinologic signs.

The only positive laboratory finding was a polycythemia with 17.8 gm. per cent hemoglobin.

The standard roentgenograms of the skull were normal.

The pneumoencephalographic study showed, however, marked distention of the lateral ventricles.

A midline air-containing structure measuring approximately 4.5 cm. in width by 4.5 cm. in height was demonstrated above the sella turcica (Fig. 1). There was a dense outline conforming exactly to the contour of the third ventricle with respect to the underlying cystic mass. The third ventricle accompanied this cystic lesion up to the inferior and chiasmatic area (Fig. 2). This suprasellar subarachnoid cyst was therefore clearly delineated by the third ventricle.

The patient was operated upon.

In the infrachiasmatic area, the shell of the cyst was indentified. It appeared white and measured over 1 mm. in thickness.

The cyst and the chiasmatic cistern were emptied. By cauterization, a marsupialization into the chiasmatic cistern was produced. There was excellent postoperative recovery.

Histologically, an edematous disassociated glial tissue on one side, with avascularized, conjunctival lining on the other was found (Fig. 3).

CASE II. This 25 year old female also was admitted because of headaches. However, her history revealed primary amenorrhea, nanism and dry skin. The endocrinologic study showed normal 17-ketosteroids, but the 17-hydroxycorticosteroids were reduced to 0 and the creatinemia was lowered.

* From the Departments of Radiology, † Neurology, ‡ Pathology, § Medicine, ‖ and Neuro-Surgery, ¶ the Maisonneuve Hospital, Montreal, Quebec, Canada.

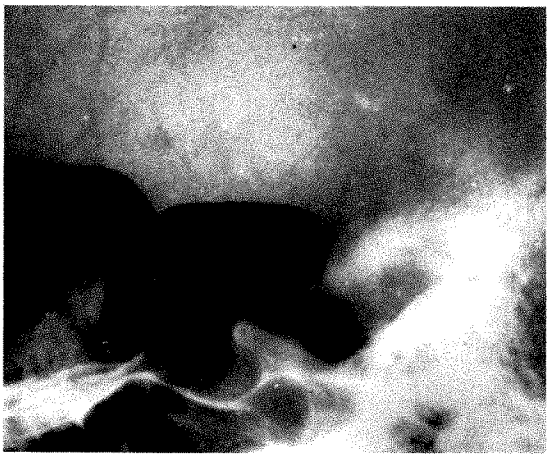


Fig. 2. *Suprasellar subarachnoid cyst of presumed cisternal origin.* Submentovertical position with horizontal rays. The anterior portion of the cyst is well dissociated from the inferoanterior portion of the third ventricle (arrows).

There was optical atrophy of the right eye and a bilateral inferotemporal quadranopsia indicating a chiasmatic lesion.

The lumbar puncture revealed an elevated cerebrospinal fluid pressure of 474.

The standard skull roentgenograms demonstrated definite modifications in the appearance of the sella turcica which were also well visualized in the pneumoencephalographic study (Fig. 4). The dorsum sella was markedly altered and its upper portion had nearly disappeared. The anterior clinoids were everted and elevated. The more conspicuous modification, however, was the changed appearance of the clivus, which resembled an inverted figure of 3 with horizontalization of its upper portion. There was evidence of a slight platybasia without basilar impression. Finally, the occipital emissary vein was dilated indicating intracranial hypertension.

Pneumoencephalography showed the tonsils slightly under the foramen magnum (Fig. 4) and the fourth ventricle lowered. The pontine cistern was well visualized, as was what appeared to be the interpeduncular cistern (Fig. 5). The ambiens cistern was also considerably lowered, and the interpeduncular cistern appeared enlarged. It was not possible to localize the aqueduct. The convexity of the pericallosal cistern was accentuated in relation to the dilated ventricles.

A few days later, a ventriculographic examination was performed which confirmed the very important dilatation of both lateral ventricles. We were unable to visualize properly the third and fourth ventricles, even after repeated maneuvers. However, a small midline air-containing structure of 1 cm. diameter was demonstrated just above the sella turcica and another air-containing structure in the area of the interpeduncular cistern (Fig. 6).

A subsequent iodoventriculographic study showed the contrast material dropping into 3 loculated spaces over the sella turcica and finally into the area of the dilated interpeduncular cistern (Fig. 7 and 8). This raised the question of a possible communication between

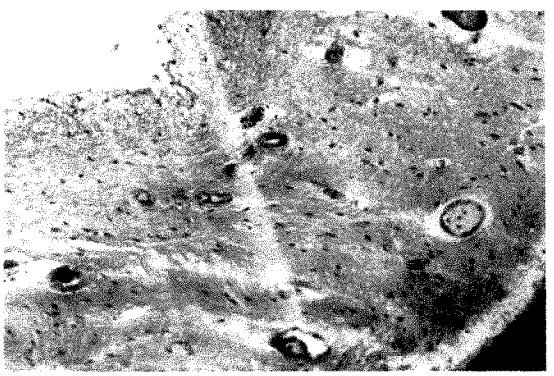


Fig. 3. *Histologic section of the suprasellar arachnoid cyst of presumed cisternal origin.* There is edematous dissociated glial tissue on one side with conjunctival lining on the other side.



Fig. 4. *Suprasellar subarachnoid cyst of presumed ventricular (third) origin.* Upright position. There is a modified dorsum sellae with horizontalization of the upper portion of the clivus (double arrows), slightly herniated tonsils, and a lowered fourth ventricle (single arrow).

an elongated foramen of Monro and the posterior dilated portion of the interpeduncular cistern.

A diagnosis of suprasellar subarachnoid cyst was suggested but we requested another pneumoencephalographic study with urea, so that the aqueduct could be visualized before this patient was operated on.

This iodoventriculographic study was performed around noon. She did relatively well and remained conscious until 8:00 P.M. when unfortunately she suddenly died.

The autopsy findings were as follows: The anterior portion of the third ventricle was dilated and its lateral borders were fused in such a way that only a very narrow and irregular pathway was left open (Fig. 9). Arising from its floor, a retro-infundibular cystic formation of 2 cm. diameter was found communicating with the anterior portion of the third ventricle (Fig. 10). The aqueduct was almost completely stenotic.

Sarcoid lesions[8] involving the third ventricle, the infundibular area, the optic chiasm, the posterior lobe of the hypophysis and the aquecuct were demonstrated histologically (Fig. 11).

DISCUSSION

On the basis of the above 2 cases and, in retrospect, of a third case we studied in the past with Drs. J. L. Léger and Hardy,[9]

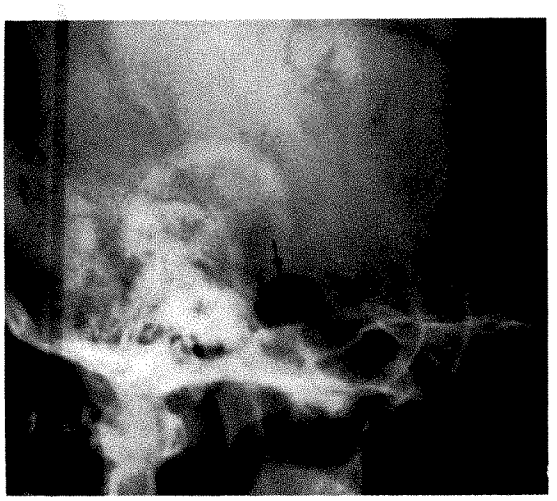


Fig. 5. *Suprasellar subarachnoid cyst of presumed ventricular (third) origin.* Upright position. There is a presumed dilated interpeduncular cistern (arrow).



Fig. 6. *Suprasellar subarachnoid cyst of presumed ventricular (third) origin.* Submentovertical position with horizontal rays. There is a small midline air collection projecting in front of the formerly described apparent interpeduncular cistern (arrow).

two types of subarachnoid cysts in the suprasellar area may be postulated.

In the First Type, the clinical signs are minimal, especially from the endocrinologic point of view. The sella turcica appears normal and, on pneumoencephalographic study, the midline air-containing cyst is well delineated from the third ventricle without elevation in the tension of the cerebrospinal fluid. The diagnosis is relatively easy and the prognosis is good, in particular if the operation is limited to marsupialization. This type might develop from the supra or retrosellar subarachnoid cisterns. In fact, stenosis of the transverse arachnoid membrane of Lilliequist in the interpeduncular cistern has already been advocated by Hardy as its possible cause.

In the Second Type, the endocrinologic signs play a significant role, as observed in our Case 11. This was a young female in whom originally we suspected a craniopharyngioma. However, in comparing the findings with those of another well documented case already reported in 1966 with Drs. J. L. Léger and Hardy, we soon real-

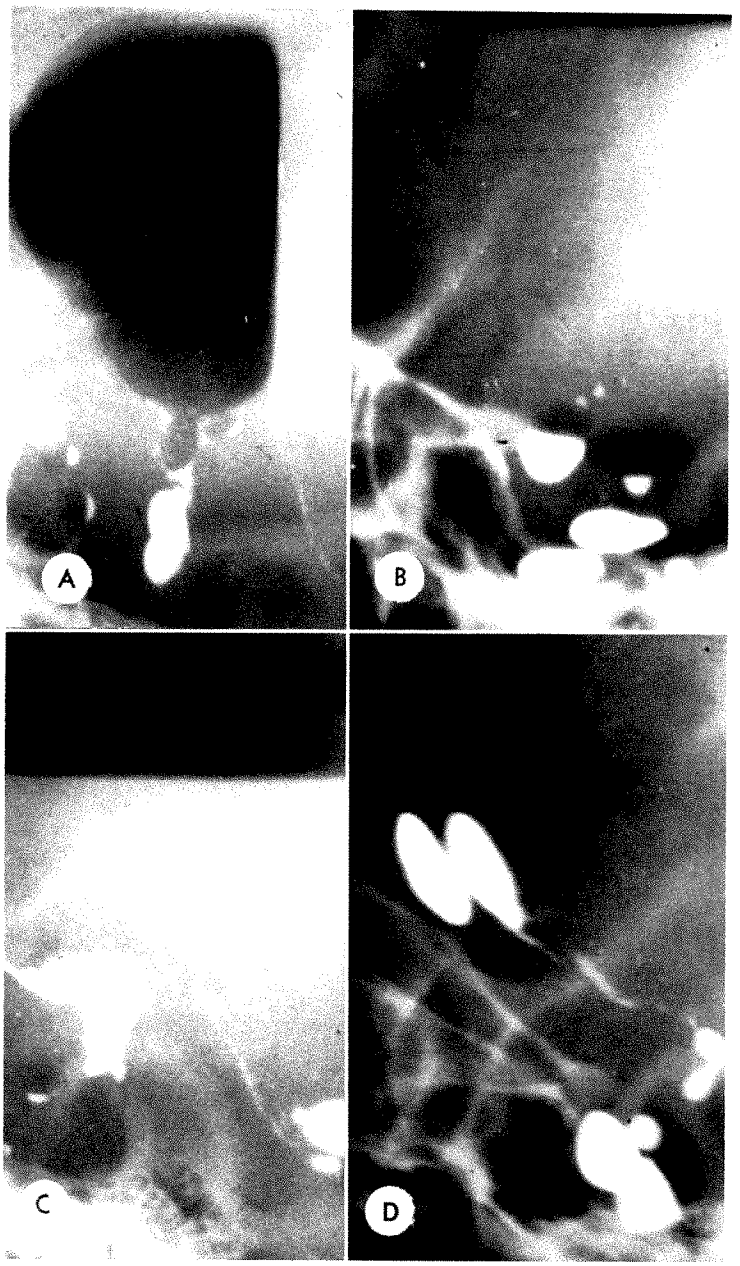


Fig. 7. *Suprasellar subarachnoid cyst of presumed ventricular (third) origin.* (*A–D*) Ventriculography; horizontal ray examination with different positions of the head. Note contrast material dropping in 3 loculated spaces over the sella turcica.

ized that both had endocrinologic signs. Both presented a certain amount of nanism, amenorrhea and a retarded skeletal development. The creatinemia was lowered in both. These endocrinologic signs pointed towards an expansive process in the sellar area.

The sella turcica was considerably more modified in our Case II than in Case I, although both showed a slight concavity of the upper portion of the clivus.

Delineation from the third ventricle remained nearly impossible in both cases. Moreover, on the ventriculographic study,

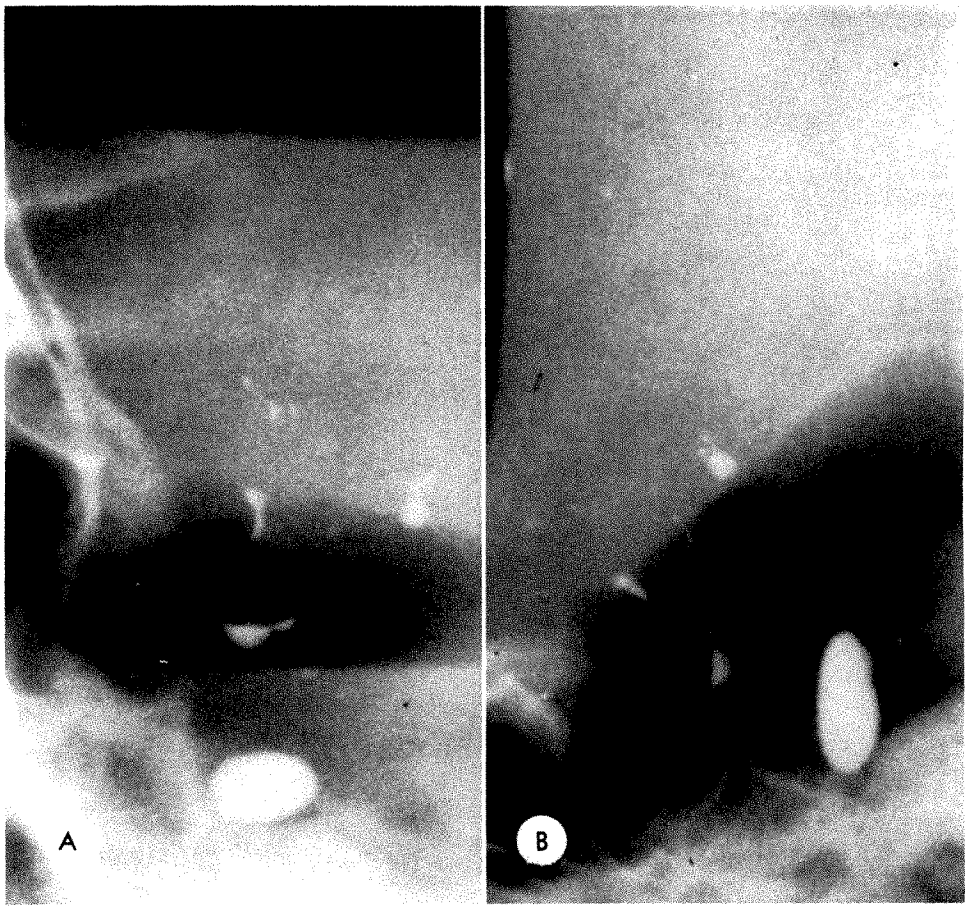


FIG. 8. *Suprasellar subarachnoid cyst of presumed ventricular (third) origin.* (*A* and *B*) Ventriculography; horizontal ray examination in extended upright and brow-up position. The contrast material finally drops from over the sella turcica down in the area of the dilated interpeduncular cistern.

a small midline air-containing area was visualized just over the sella turcica and the interpeduncular cistern was also dilated in both cases. Contrary to the First Type, the Second Type seemed to arise from the floor of the third ventricle.

Both of the patients of the Second Type had an unfortunate outcome. The first (Case II) died 8 hours after an iodoventriculographic examination and the other (Case of Léger and Hardy) remained unconscious and vegetative after being operated on. These lesions with endocrinologic signs appear, therefore, only falsely benign and our management should probably be reconsidered. Iodoventriculographic examination might precipitate herniation of the tonsils in the precariously compensated patients.

Consequently, the operations considered should be most conservative.

CONCLUSION

Two cases of suprasellar subarachnoid cysts are reported with mention of a third case for the purpose of comparison.

The following main features were noted:

1. A First Type might be isolated where the endocrinologic clinical signs are minimum and where the sella turcica remains normal. On the pneumoencephalographic study, the suprasellar subarachnoid cyst is well delineated from the third ventricle and easily demonstrated. The tension of

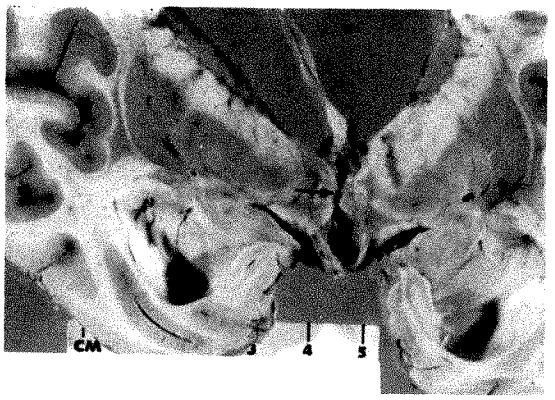


Fig. 9. *Suprasellar subarachnoid cyst of presumed ventricular (third) origin.* Autopsy; coronal section of the brain. Note apposed walls of the third ventricle of inflammatory origin (arrow).

the cerebrospinal fluid remains normal.

The evolution is good when the operation is limited to marsupialization.

This First Type might develop from the suprasellar subarachnoid cisterns.

2. A Second Type of subarachnoid cyst may be distinguished. In our Case II, as well as in another previously reported case, we were dealing with young females, with definite endocrinologic signs, mainly nanism, amenorrhea, retarded skeletal development and lowered creatinemia. These endocrinologic signs pointed to an expanding lesion in the sellar area which could have been a craniopharyngioma, an epidermoid cyst or even an ectopic pinealoma.

Both of our cases presented a modified dorsum sellae and, moreover, a concavity of the upper portion of the clivus which somewhat resembled an inverted figure of 3.

It was impossible to separate reasonably well the suprasellar subarachnoid cyst from the third ventricle.

These patients should be considered as being in a very precarious equilibrium, should be managed with great care, and perhaps sedated before a minimal intervention.

This Second Type of suprasellar subarachnoid cyst appears to develop from the floor of the third ventricle and, at least in our case, in connection with an inflammatory process.

Inflammatory processes in the area of

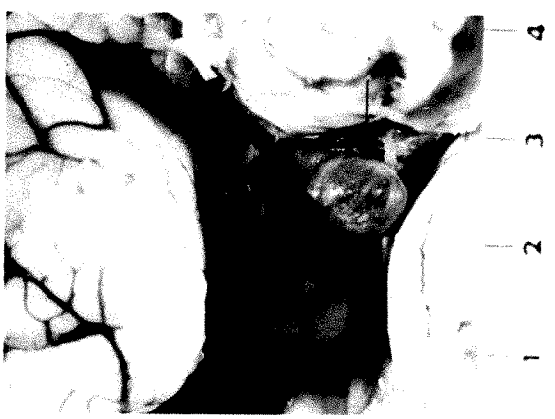


Fig. 10. *Suprasellar subarachnoid cyst of presumed ventricular (third) origin.* Autopsy; basal view of the brain. Note retro-infundibular cystic formation communicating with the anterior portion of the abnormal third ventricle (arrow).

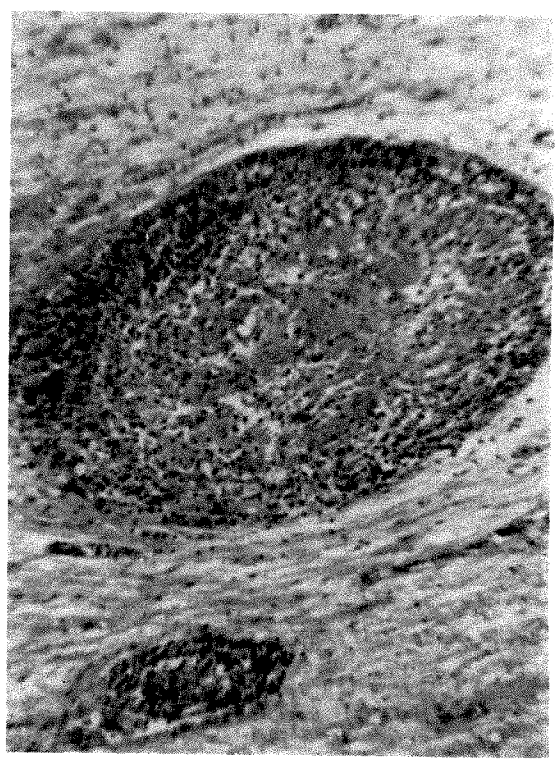


Fig. 11. *Suprasellar subarachnoid cyst of presumed ventricular (third) origin.* Autopsy; histologic section of the basal arachnoid. This demonstrates a typical sarcoid lesion.

the third ventricle should always raise suspicion of sarcoidosis or tuberculosis.[8*]

SUMMARY

Two cases of suprasellar subarachnoid cysts are reported.

Case I. The clinical symptoms of Case I consisted only of postural headaches. The midline suprasellar air-containing structure visualized on the pneumoencephalographic study was well delineated from the third ventricle and the patient did well after a limited operation (marsupialization).

This type of suprasellar subarachnoid cyst might develop from the suprasellar subarachnoid cisterns.

Case II. Nanism, amenorrhea, retarded skeletal development together with lowered creatinemia and 17 hydroxy-corticosteroids were the main clinical signs in Case II. They were associated with a bilateral inferotemporal quadrantanopsia.

Case II was compared with a nearly similar case already reported by Hardy and associates before the Canadian Neurological Society in June 1966.

Both had a modified dorsum sellae with an inverted figure of 3 appearance of the clivus.

Both had an important air-containing expanding lesion in the midline impossible to separate properly from the third ventricle.

Both had an unfortunate outcome.

This type of suprasellar subarachnoid cyst appears to develop from the floor of the third ventricle, sometimes in connection with an inflammatory process.

Based on these cases, the radioclinical features were determined. A strong plea is made to radiologists to keep in mind the possibility of a complicated suprasellar subarachnoid cyst developing from the floor of the third ventricle with an inflammatory component.

Sarcoidosis or tuberculosis should always be thought of in this area.

When the roentgenologic changes would normally point to a craniopharyngioma, especially if the clivus has an inverted figure of 3 appearance, this diagnosis should be considered.

*This paper is presented as a "work in progress" and should be looked upon as a further approach to a more precise description of an incompletely known suprasellar neurologic entity. It is, therefore, liable to revision in the future.

André Sansregret, M.D.
Department of Radiology
Maisonneuve Hospital
5415 l'Assomption Boulevard
Montreal 36
Quebec, Canada

REFERENCES

1. Askanazy, C. L. Sarcoidosis of the central nervous system. *J. Neuropath. & Exper. Neurol.*, 1952, *11*, 392–400.
2. Chynn, K.-Y. Neuroradiologic exploration in intra and parasellar conditions. *Radiol. Clin. North America*, 1966, *4*, 93–115.
3. Höök, O. Sarcoidosis with involvement of nervous system: report of nine cases. *A.M.A. Arch. Neurol. & Psychiat.*, 1954, *71*, 554–575.
4. Jefferson, M. Sarcoidosis of nervous system. *Brain*, 1957, *80*, 540–556.
5. Kier, E. L. Infantile sella turcica: new roentgenologic and anatomic concepts based on developmental study of sphenoid bone. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1968, *102*, 747–767.
6. Neuhauser, E. B. D. Mucopolysaccharidoses. Presented at the Albert Einstein College of Medicine Postgraduate Course in Radiology of the Skeletal System. New York, May 15–17, 1967.
7. Ring, B. A., and Waddington, M. Cysts of sella turcica. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1966, *98*, 611–615.
8. Robert, F. Sarcoidosis of central nervous system: report of case and review of literature. *A.M.A. Arch. Neurol. & Psychiat.*, 1962, *7*, 442–449.
9. Sansregret, A., Léger, J. L., Hardy, J., and Robillard, R. Kystes Arachnoidiens de la Région Sellaire. Presented at the Congress of the Canadian Society of Radiology, March, 1966.
10. Selenkow, H. A., Tyler, H. R., Matson, D. D., and Nelson, D. H. Hypopituitarism due to hypothalamic sarcoidosis. *Am. J. M. Sc.*, 1959, *238*, 456–463.

CONGENITAL ARACHNOID CYSTS*

By YAHYA M. BERKMEN, M.D.,† JACK BRUCHER, M.D.,† *and* JAMES H. SALMON, M.D.‡
CINCINNATI, OHIO

INTRACRANIAL cysts lined by arachnoid-like membrane are space-occupying lesions and may cause hydrocephalus, local bulging of the skull, displacement of the brain, convulsions, and a variety of neurologic symptoms. Although they usually manifest themselves in infancy or childhood, these cysts may remain latent for many years or even be an incidental autopsy finding.

Arachnoid cysts are either congenital (primary) or acquired (secondary).[15] Acquired arachnoid cysts result from previous infection, trauma, or hemorrhage. The mechanism for formation of traumatic and inflammatory cysts has been adequately described and a distinction made between subdural hygroma and acquired arachnoid cyst.[6,9,20] When there is no evidence of traumatic or inflammatory origin, the cysts are considered to be congenital. The wall of congenital cysts consists of a thin layer of connective tissue which does not adhere to adjacent structures. There is no significant capillary proliferation or hemosiderin deposition as is frequently noted in subdural hematoma membranes. The cyst fluid is usually clear and colorless with a variable protein content but may occasionally be xanthochromic.[3,19] Cysts lined by ependymal cells[7] and those containing choroid-like tissue[13] or neuroglial tissue[2] should not be classified as arachnoid cysts.

The plain roentgenograms in cases of arachnoid cyst may be normal or show a localized thinning or bulging of the skull. Pneumography demonstrates a space-occupying lesion which, on angiography, will prove to be avascular.

REPORT OF CASES

CASE 1. This 5½ month old boy was admitted to the Children's Hospital, Cincinnati, because of an enlarging head. Maternal pregnancy and delivery were normal. There was no history of vomiting or convulsions.

On physical examination, the anterior fontanelle was slightly tense. Fundoscopic examination was normal except for some pallor of the disk. His eyes did not follow a light.

Bilateral subdural taps were negative. Ventriculograms (Fig. 1, *A* and *B*) showed communicating hydrocephalus and indentation of the posterior portion of the third ventricle. The midbrain appeared rotated and displaced to the left. The right cerebellopontine cistern did not fill with air. The significance of these

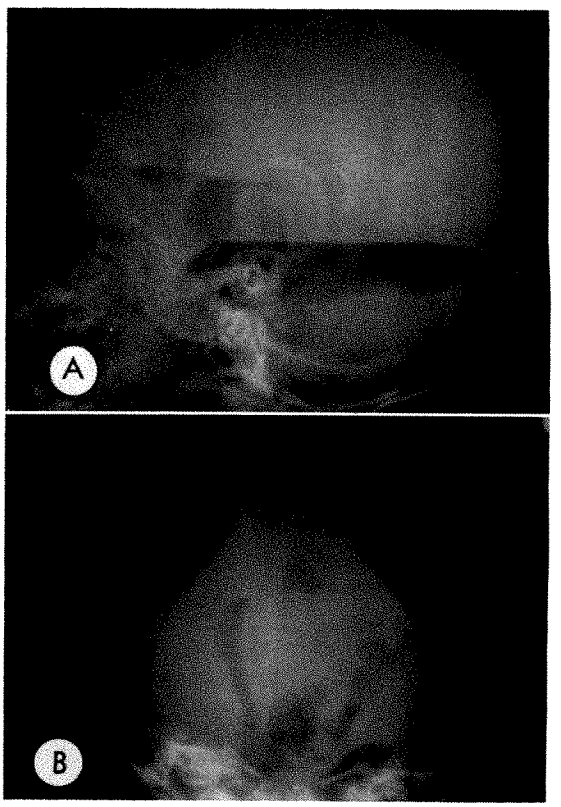


FIG. 1. Case 1. (*A*) Lateral view during ventriculography in hanging-head position shows communicating hydrocephalus. Note the indentation of the posterior portion of the third ventricle. (*B*) Towne's view. The lateral ventricles are dilated. The right cerebellopontile angle is not filled with air. The midbrain is rotated and shifted to the left.

* From the Departments of Radiology,† and Neurosurgery, ‡ University of Cincinnati College of Medicine, Cincinnati, Ohio.

findings was not appreciated at that time. A right-sided ventriculo-atrial shunt using a normal pressure Holter valve was done.

The patient did well, but 5 months postoperatively the head circumference had increased 3 cm. The shunt appeared to be functioning properly. The child was readmitted to change the normal pressure valve to a lower pressure one.

Repeat ventriculography showed no change. Three days later he became febrile and died. Cultures of the cerebrospinal fluid were sterile.

At autopsy the brain weighed 925 grams. The meninges were unremarkable. The most significant finding was a large cystic mass displacing the brainstem markedly to the left. The cyst ruptured during removal of the brain. Projecting into cystic space was another cystic structure 3.5 cm. in diameter which appeared to be attached to the right cerebellar hemisphere (Fig. 2).

The ventricles were moderately enlarged without evidence of ventriculitis. The brainstem was greatly distorted due to angulation, which was greatest at the pontomedullary junction. Histologic section of the cyst wall is illustrated in Figure 3 and reveals a thin connective tissue wall.

Case II. This 3 month old infant was born after an uncomplicated pregnancy and delivery. The pediatrician had noticed gradual enlargement of the head and the child showed increased irritability prior to admission to the Children's Hospital. On physical examination the fontanelle was tense. The head circumference was 45 cm., which is greater than the 97th percentile.

Bilateral subdural taps were negative. A ventriculogram (Fig. 4) was interpreted as showing aqueduct stenosis. Retrospectively, elevation and forward displacement of the posterior portion of the third ventricle were present. A ventriculo-atrial shunt was performed and a medium pressure Holter valve was inserted. The shunt was revised on three occasions because of malfunction.

The patient was readmitted a year later because of a temperature of 105° F., cough, and

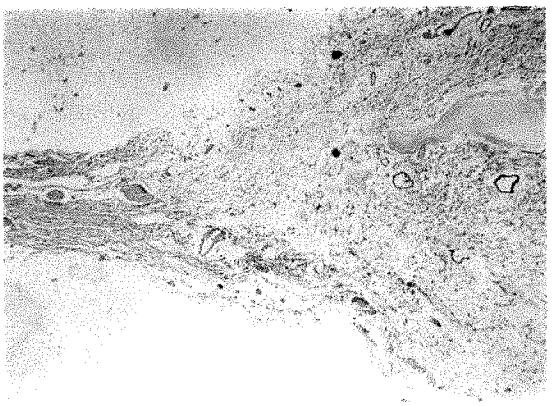


Fig. 3. Case I. Microscopic section of the cyst wall consisting of connective tissue and blood vessels. The left side of the specimen is in cross-section, whereas the right side is cut parallel to the surface of the cyst (×150).



Fig. 2. Case I. Basal view of the brain after removal. A cyst, 3.5 cm. in diameter, is seen at the right pontomedullary angle. A large empty space lateral to the cyst was occupied by a larger cyst which ruptured during removal of the brain. The brainstem is markedly displaced to the left and rotated.



Fig. 4. Case II. Brow-down, lateral view of the skull during ventriculography. The occipital horns and the third ventricle are dilated. There is elevation and forward displacement of the posterior portion of the third ventricle.

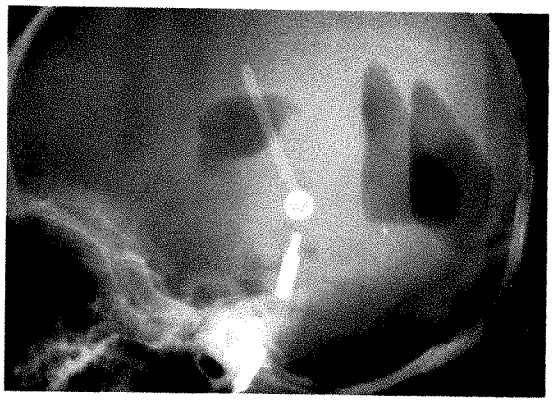


FIG. 5. Case II. After shunting procedure. No significant change is seen. A Holter valve is in the right lateral ventricle.

rhinorrhea. The neurologic examination was normal. The fontanelle was soft and the shunt appeared to be functioning.

Ventriculography was repeated and no significant change was seen (Fig. 5). Pneumoencephalography (Fig. 6, *A–C*) outlined a large mass on the right side protruding into the right lateral ventricle. Its medial border crossed the midline. Air was present within the mass. Right brachial angiography (Fig. 7, *A* and *B*) showed distortion of the midbrain, hydrocephalus, and elevation of the sylvian group of arteries.

Through a posterior parietal exposure and a transcortical incision, a 3×4 cm. bulge was seen on the medial wall of the right ventricle. This was traversed by the choroid plexus as well as by the ventricular catheter. A centimeter of the medial wall of the ventricle was excised and a thin-walled cyst was encountered. A needle introduced into this area obtained crystal-clear fluid. The cyst was fenestrated and avulsed. The histologic report was nonspecific membranous tissue consistent with arachnoid tissue. Postoperatively the patient did well.

CASE III. This patient was admitted to the Cincinnati General Hospital at the age of 10 months because of an enlarging head. Three days prior to admission he became irritable. There was one episode of vomiting. The child's development was obviously retarded and he could not sit without support or hold his head erect.

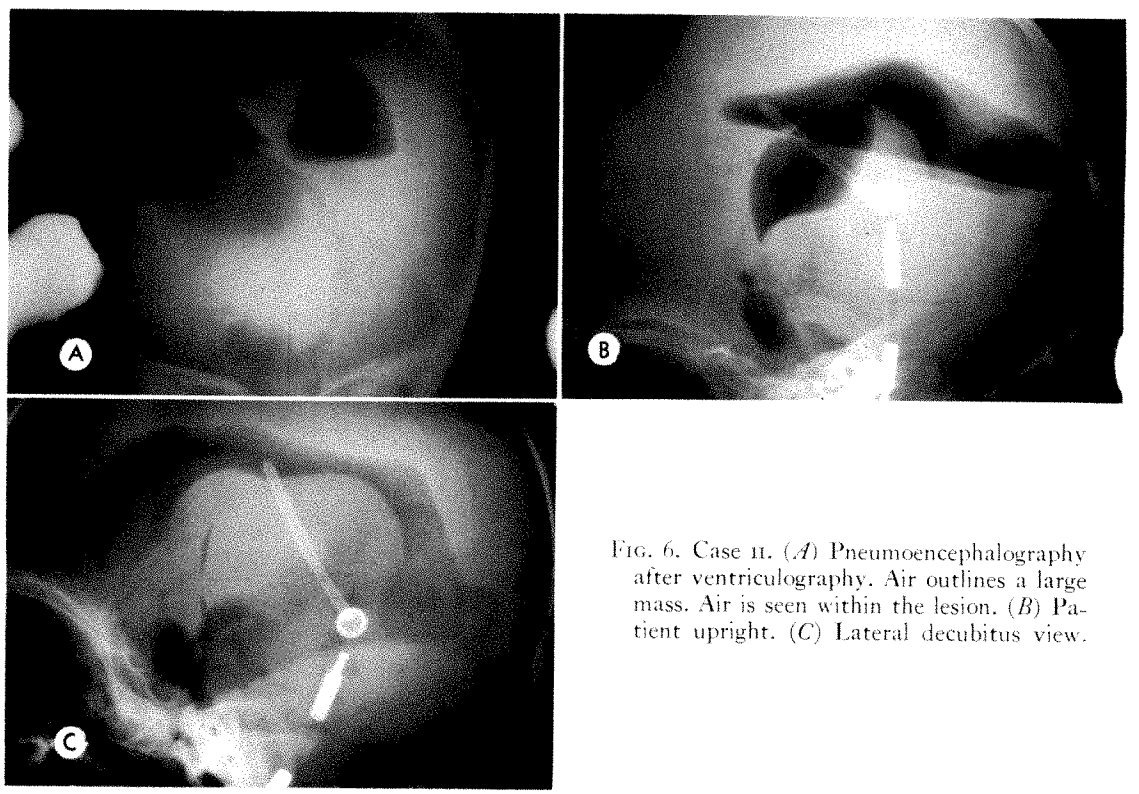


FIG. 6. Case II. (*A*) Pneumoencephalography after ventriculography. Air outlines a large mass. Air is seen within the lesion. (*B*) Patient upright. (*C*) Lateral decubitus view.

Physical examination revealed a widely patent fontanelle and venous distention over the scalp. The head circumference was 49 cm., the 97th percentile. There was no papilledema and the pupils reacted to light. The electroencephalogram was interpreted as normal. The child was discharged with a diagnosis of arrested hydrocephalus.

He was readmitted at 13 months of age for further studies. The head circumference had remained stable; however, development was still retarded.

Diagnosis of a left temporal lobe mass was made on ventriculography (Fig. 8, *A* and *B*) and angiography (Fig. 9, *A* and *B*). A positive contrast study showed patency of the aqueduct and fourth ventricle. A ventriculo-atrial shunt was made to control the hydrocephalus. Two

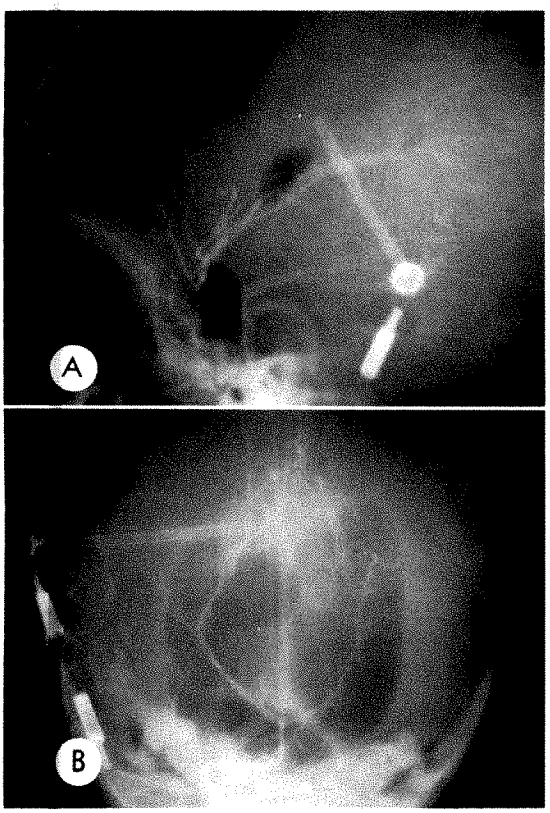


FIG. 7. Case II. (*A*) Right brachial angiography, lateral projection. The sweep of the anterior cerebral artery is enlarged. The sylvian group of arteries are elevated. Avascular nature of the lesion is noted. (Air in the ventricles and in the cyst is from previous air studies.) The right posterior cerebral artery is slightly lower than the left. (*B*) Anteroposterior view. A gentle curve between P 1 and P 2 is lost on the right side. These two parts are blended in a steep upward displacement. P 3 and P 4 are stretched and form a curve with concavity laterally. The temporal branches are splayed and the occipital branches are crowded.

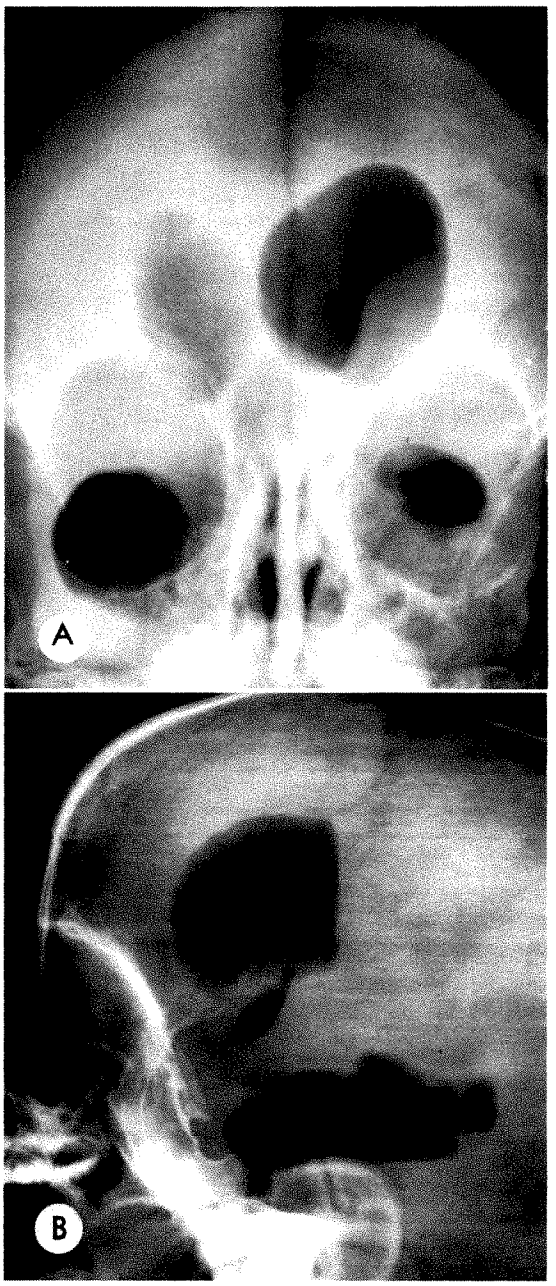


FIG. 8. Case III. (*A*) Ventriculography, anteroposterior projection. There is bilateral hydrocephalus. The left temporal horn is slightly elevated. (*B*) Lateral projection. Amputation of the front of the left temporal horn is clearly seen. There is indentation of the anterior portion of the third ventricle from below.

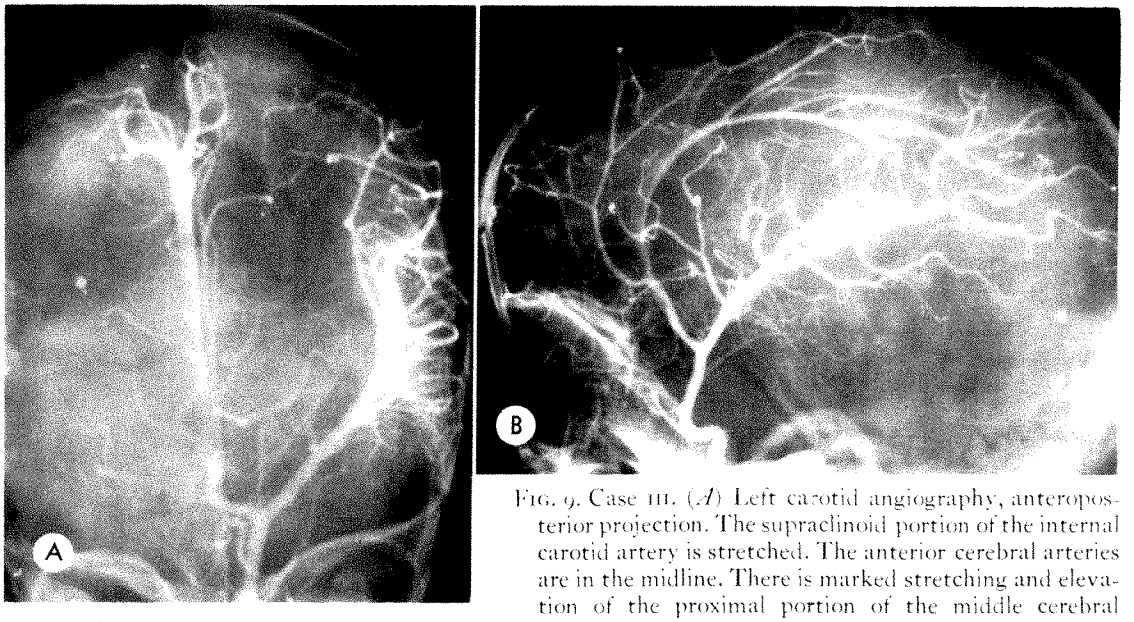


FIG. 9. Case III. (*A*) Left carotid angiography, anteroposterior projection. The supraclinoid portion of the internal carotid artery is stretched. The anterior cerebral arteries are in the midline. There is marked stretching and elevation of the proximal portion of the middle cerebral artery. The "knee" is also elevated. (*B*) Lateral projection. Elevation and stretching of the supraclinoid portion of the internal carotid artery are seen. The sylvian group of arteries are curved and there is "draping" of some of the peripheral branches.

weeks later a left temporal craniectomy was performed. As the bone was removed the dura appeared unusually blue. On excising the dura a large cyst ruptured through the defect. The wall was thin and biopsy was interpreted as consistent with an arachnoid membrane. The cyst displaced the temporal lobe superiorly and posteriorly. It seemed to occupy most of the middle fossa. When it was emptied, the incisura of the tentorium could be visualized. The patient did well postoperatively but was lost to follow-up.

DISCUSSION

The theory that arachnoid cysts could be a developmental error has been suggested[8] and convincing evidence of this has come from the work of Starkman *et al.*,[19] who showed that these cysts are intra-arachnoid rather than subarachnoid and are separated from the pia by subarachnoid space. Subsequent authors have confirmed the intra-arachnoid location of these cysts.[3,10,18,22]

Robinson[16,17] reported 7 cases of large arachnoid cysts occupying the temporal fossa associated with an agenetic temporal lobe. He also found 15 more cases in the literature described as subdural hygromas. He believed the primary pathology was agenesis of the temporal lobe and noted that other coexisting anomalies such as agenesis of the frontal lobe, anterior encephalocele, absence of the posterior orbital wall, and absence of the internal carotid artery have also been described in this condition.

Congenital arachnoid cyst is often symptomatic, presenting with signs and symptoms of a space-occupying lesion.[1,4,17] Bulging of the skull associated with thinning of the diploic space is not a specific finding for this type of cyst; in fact, it was not present in any of our cases. Chronic subdural hematoma, porencephalic cyst, unilateral hydrocephalus, slow-growing glioma, intracranial aneurysm and neurofibromatosis may also cause calvarial thinning.[5,9,20]

The cyst shows no sex preference, nor predilection of side. It may be infratentorial,[1,14] over the convexity of the brain, parasagittal,[3] intrasylvian,[3,10,21] suprasellar,[4,8] or arise from the quadrigeminal plate[12,14] or cisterna ambiens.[11]

The cyst usually does not communicate with the ventricle or subarachnoid space;[1, 10,19,22] therefore, it rarely fills on pneumography and an absolute roentgen diagnosis cannot be made.

In Case II, pneumoencephalography one year after the shunt showed air in the cyst. The pathway of entry of the air was unexplained, even after operation.

Angiographic studies have seldom been performed in these patients. They show an avascular lesion and displacement of adjacent vessels. Radiologic localization of the cyst is not difficult. Those arising from the quadrigeminal plate typically elevate the posterior portion of the third ventricle and displace it anteriorly. The suprapineal recess is not obliterated but is bowed around the cyst.[14]

Hydrocephalus is almost always present in symptomatic patients. Infratentorial cysts and those arising from the quadrigeminal plate result in more severe and earlier hydrocephalus than those located over the convexity or in the middle fossa because of the pressure they exert on the aqueduct or fourth ventricle. All 3 of our cases showed evidence of internal hydrocephalus, which was more marked in Case II and Case III than in Case I. The hydrocephalus in Case I was thought to be due to tentorial block.

Patency of the aqueduct and fourth ventricle is readily demonstrated in posterior fossa and quadrigeminal plate cysts. If air fails to enter the aqueduct and fourth ventricle after ventriculography, in spite of the various maneuvers, pneumoencephalography or positive contrast studies are necessary to rule out aqueduct occlusion.

The importance of early recognition of this condition cannot be overemphasized, as these are benign lesions and normal intelligence and development can be expected if the cysts are excised before permanent brain damage occurs. Ideally, the cysts should be resected completely. Ventriculostomy may be performed if there is recurrence, and a shunting procedure may later be necessary if hydrocephalus is not relieved because of late occlusion of the aqueduct.[3] In all our patients, shunting procedure preceded the exploration. A good result was obtained in Case II and Case III. The first patient died before exploration could be done.

SUMMARY

Three cases of congenital arachnoid cysts are discussed. They all presented with hydrocephalus. The benign nature and the importance of early surgical intervention are emphasized.

More severe hydrocephalus results from the posterior fossa and quadrigeminal plate cysts because of pressure on the aqueduct and the fourth ventricle. Therefore, every effort must be made to demonstrate the patency of these structures during air studies. In cases of failure, positive contrast study is indicated. Indentation and anterior displacement of the posterior portion of the third ventricle, and elevation of the suprapineal recess are important clues for the diagnosis of the cysts of the quadrigeminal plate and for infratentorial cysts with supratentorial extension.

Jack Brucher, M.D.
Department of Radiology
Cincinnati General Hospital
Cincinnati, Ohio 45229

REFERENCES

1. Alexander, E., Jr. Benign subtentorial supracollicular cyst as a cause of obstructive hydrocephalus. Report of a case. *J. Neurosurg.*, 1953, *10*, 317–323.
2. Alvord, E. C., Jr., and Marcuse, P. M. Intracranial cerebellar meningo-encephalocele (posterior fossa cyst) causing hydrocephalus by compression at the incisura tentorii. *J. Neuropath. & Exper. Neurol.*, 1962, *21*, 50–69.
3. Anderson, F. M., and Landing, B. H. Cerebral arachnoid cysts in infants. *J. Pediat.*, 1966, *69*, 88–96.
4. Barlow, A. Suprasellar arachnoid cyst. *Arch. Ophthal.*, 1935, *14*, 53–60.
5. Childe, A. E. Localized thinning and enlargement of the cranium: with special reference to the middle fossa. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1953, *70*, 1–21.
6. Dandy, W. E. Treatment of an unusual subdural

hygroma (external hydrocephalus). *Arch. Surg.*, 1946, *52*, 421–428.

7. HAMBY, W. B., and GARDNER, J. An ependymal cyst in the quadrigeminal region. Report of a case. *Arch. Neurol. & Psychiat.*, 1935, *33*, 391–398.
8. HAMBY, W. B., and GARDNER, J. Visualization of suprasellar tumors by encephalography: report of nine cases. AM. J. ROENTGENOL. & RAD. THERAPY, 1935, *33*, 1–9.
9. HARDMAN, J. Asymmetry of the skull in relation to subdural collections of fluid. *Brit. J. Radiol.*, 1939, *12*, 455–461.
10. HOLST, S. Congenital intracranial arachnoidal cyst. Case reports and discussion of the pathogenesis. *J. Oslo City Hosp.*, 1965, *15*, 113–120.
11. KATAGIRI, A. Arachnoidal cyst of the cisterna ambiens: report of two cases. *Neurology*, 1960, *10*, 783–786.
12. KRUYFF, E. Paracollicular plate cysts. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1965, *95*, 899–916.
13. LEWIS, A. J. Infantile hydrocephalus caused by arachnoid cyst: case report. *J. Neurosurg.*, 1962, *19*, 431–434.
14. LOURIE, H., and BERNE, A. S. Radiological and clinical features of an arachnoid cyst of the quadrigeminal cistern. *J. Neurol., Neurosurg. & Psychiat.*, 1961, *24*, 374–378.
15. OLIVER, L. C. Primary arachnoid cysts: report of two cases. *Brit. M. J.*, 1958, *1*, 1147–1149.
16. ROBINSON, R. G. Intracranial collections of fluid with local bulging of the skull. *J. Neurosurg.*, 1955, *12*, 345–353.
17. ROBINSON, R. G. Local bulging of the skull and external hydrocephalus due to cerebral agenesis. *Brit. J. Radiol.*, 1958, *31*, 691–700.
18. SCHREIBER, M. S. Primary congenital arachnoid cysts. *Med. J. Aust.*, 1959, *2*, 802–803.
19. STARKMAN, S. P., BROWN, T. C., and LINELL, E. A. Cerebral arachnoid cysts. *J. Neuropath. & Exper. Neurol.*, 1958, *17*, 484–500.
20. TAVERAS, J. M., and RANSOHOFF, J. Leptomeningeal cysts of the brain following trauma with erosion of the skull: study of seven cases treated by surgery. *J. Neurosurg.*, 1953, *10*, 233–241.
21. WEINMAN, D. F. Arachnoidal cysts in the sylvian fissure of the brain. *J. Neurosurg.*, 1965, *22*, 185–187.
22. WILSON, C. B., and BERTAN, V. Cerebral leptomeningeal cysts of developmental origin. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1966, *98*, 570–574.

VOL. 105, NO. 2

POST-TRAUMATIC LEPTOMENINGEAL CYSTS*

By FRANK H. GRUBER, M.D.
CHARLESTON, SOUTH CAROLINA

AN UNUSUAL complication of childhood skull fractures is a post-traumatic leptomeningeal cyst which presents a characteristic erosion of the skull on roentgenograms. These lesions may or may not cause symptoms. Cysts due to postinflammatory changes and developmental abnormalities will not be considered in this report.

REPORT OF CASES

CASE I. At age 7 weeks this child fell from his father's arms, suffering a right parietal skull fracture with 4 mm. of diastasis (Fig. 1). Four months later, on routine follow-up examination, an 8 cm.×2 cm. pulsating defect was palpable along the fracture site (Fig. 2). There was no mass protruding beyond the margins of the skull. The physical examination was otherwise negative and the patient was asymptomatic. At surgery, a dural defect larger than the bone defect was found. The former was closed with a dural graft and the latter with a methyl methacrylate plastic. The patient remained asymptomatic.



FIG. 1. Case I. A diastotic right parietal fracture is present, occurring at age 7 weeks.



FIG. 2. Case I. Four months later an irregular, scalloped defect has appeared along the fracture line with sclerotic margins.

CASE II. This child sustained a left posterior parietal fracture at the age of $3\frac{1}{2}$ months. Diastasis along the fracture line was 4 mm. (Fig. 3). The nature of the injury was not certain. During the first 3 days in the hospital the child was pale and lethargic with a bulging anterior fontanelle. Neurologically, the examination was negative except for a deviation of the eyes to the left. Copious quantities of subdural fluid were drained from the anterior fontanelle. Steady improvement allowed the patient to be discharged in good condition after $2\frac{1}{2}$ weeks. The second admission was at age of 8 months, $4\frac{1}{2}$ months after the injury. A large pulsating mass was present at the fracture site. Roentgenograms showed a 6×7 cm. bone defect (Fig. 4 and 5). The patient was asymptomatic and the neurologic examination was negative. At surgery an arachnoid cyst was found under the dural defect. The cyst was removed and the dural defect was repaired with a pericranial patch graft.

During the next 2 weeks fluid progressively

* From the Department of Radiology, Medical College of South Carolina, Charleston, South Carolina.



FIG. 3. Case II. A diastotic left posterior parietal skull fracture occurred at age 3½ months.

accumulated and drained from under the scalp flap. The patient was again taken to surgery and a 1 mm. defect in the dural suture line was found. A water-tight dural repair was accomplished, using a small piece of muscle stump. The second postoperative course was benign.

DISCUSSION

The skull defect is always associated with a dural tear and it has been suggested that the arachnoid herniates through this tear into the fracture line. The dura is absent at the center of the bone defect and adherent to the arachnoid at the margins. Due to surrounding adhesions, and a probable ball-valve mechanism, an arachnoid cyst is formed which transmits pulsations from the brain to the skull producing bone erosion.[6] The initiating fracture occurs in early infancy, usually under the age of 3 years.[2] A case in which the injury occurred at age of 6 years has been reported[6] and in only one instance has a leptomeningeal cyst been reported in an adult.[5] Bone defects appear from 4 months to many years after the fracture has occurred. Apparently, the most benign leptomeningeal cyst reported in the literature is our Case 1, in which there was not only a lack of symptoms, but also an absence of a visible or palpable mass. A small defect was detected by palpation along the frac-



FIG. 4. Case II. Four and one-half months after the skull fracture, a leptomeningeal cyst has formed, displacing the tables outward. The old fracture line can be seen anterior to the defect.

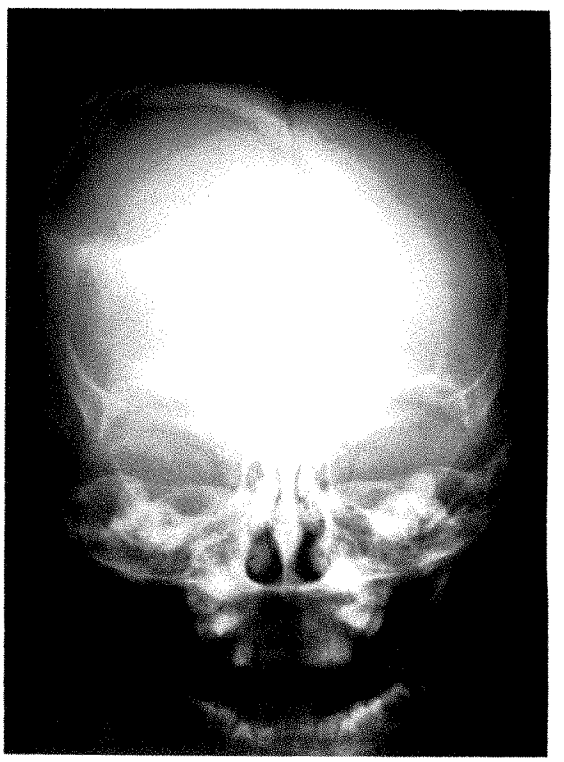


FIG. 5. Case II. The scalloped, sclerotic margins of the bone defect can be seen.

ture line on a routine follow-up examination.

Case II represents another group in which the complaint is a swelling under the scalp. Some authors report severe symptoms such as epilepsy, hemiparesis, hemiatrophy, and intense localized pain.[1,2,3,6] Fractures likely to develop leptomeningeal cysts are those with a diastasis of 4 mm. or more.[6] Most cysts are found in the posterior part of a parietal bone. Roentgenographically, the bone defect is an elongated area of lucency, aligned with the course of the old fracture which may still be seen at one end of the erosion. The margins are usually scalloped and sclerotic and occasionally there is increased vascularity in the area.[6] Large cysts balloon the bone tables outward with the central erosion involving the inner table more than the outer. Dermoid or epidermoid tumors could be confused with leptomeningeal cysts when they present lucencies with scalloped, sclerotic margins. A residual fracture line and the history of a fracture establish a leptomeningeal cyst. Displacement of the inner table toward the brain, or islands of bone debris in the defect, indicate an epidermoid tumor. Dermoids arising in the meninges may displace the inner table outward and be confusing.[4] In this case the diagnosis can be more firmly established by injecting the mass with air, outlining the multiloculated cystic spaces which do not communicate with the ventricular system or adjacent arachnoid space.[6]

Treatment consists of a water-tight repair of the dural lesion. Some surgeons repair the skull defect as well.

SUMMARY

Leptomeningeal cysts are complications of skull fractures in children, often producing epilepsy and neurologic disability.

It is interesting and fortunate that, even though these are rare lesions, the radiologist usually makes the correct diagnosis. This is due to the characteristic roentgenographic appearance.

Department of Radiology
Medical College Hospital
Medical College of South Carolina
55 Doughty Street
Charleston, South Carolina 29401

REFERENCES

1. Cooperstock, M. Leptomeningeal cyst associated with hemiplegia and skull defect of traumatic origin. *J. Pediat.*, 1946, *28*, 488–492.
2. Lende, R. A., and Erickson, T. C. Cranial defects developing at fracture sites in children. *Tr. Am. Neurol. A.*, 1959, *84*, 130–132.
3. Low, N. L., and Correll, J. W. Head pain due to leptomeningeal cysts. *Brit. J. Surg.*, 1966, *53*, 791–793.
4. Schwartz, C. W. Leptomeningeal cysts from roentgenological viewpoint. Am. J. Roentgenol. & Rad. Therapy, 1941, *46*, 160–165.
5. Soule, A. B., Jr., and Whitcomb, B. B. Extensive erosion of base of skull from leptomeningeal cyst: report of case. *Arch. Neurol. & Psychiat.*, 1946, *55*, 382–387.
6. Taveras, J. M., and Ransohoff, J. Leptomeningeal cyst of brain following trauma with erosion of skull. *J. Neurosurg.*, 1953, *10*, 233–241.

CARTILAGINOUS TUMORS OF THE BASE OF SKULL*

By HIDEYO MINAGI, M.D., *and* THOMAS H. NEWTON, M.D.
SAN FRANCISCO, CALIFORNIA

ALTHOUGH intracranial cartilaginous tumors are distinctly uncommon, 3 patients with such tumors have been seen at the University of California Medical Center within a 2 year period. In all 3 patients the tumor arose from the base of the skull. Since tumors of this type should be included in the differential diagnosis of neoplasms about the base of the skull, the clinical and roentgenographic findings in these 3 patients are presented.

REPORT OF CASES

CASE I. This 47 year old woman developed diplopia and mild ataxia 15 years before admission. At that time a tentative diagnosis of clivus chordoma was made. A third ventriculostomy was performed for relief of obstructive hydrocephalus, but the tumor was not biopsied. Following surgery the patient received a course of external irradiation. Before admission to the University of California Medical Center, the ataxia increased and was associated with bifrontal headache and loss of memory. Some slurring of speech and tinnitus were noted.

On physical examination, bilateral third, sixth, eighth, and ninth cranial nerve palsies were present, in addition to cerebellar and pyramidal signs.

Roentgenograms of the skull revealed a densely calcified 2×3 cm. mass behind the clivus (Fig. 1, *A* and *B*). No bone destruction was apparent. On vertebral arteriography, the basilar artery was displaced posteriorly around the calcified prepontine mass (Fig. 1*C*). No tumor blush or abnormal vessels were noted. A transclival craniotomy with subtotal resection of a prepontine, hard, multilobulated tumor was performed. The patient did not regain consciousness and died 12 days after the operation. At postmortem examination the residual tumor was seen to be entirely extradural and of cartilaginous consistency. Histologically the tumor consisted of well differentiated cartilage, of which a major portion had undergone either mucoid degeneration or calcification. The final pathologic diagnosis was chondroma of the clivus compressing the brain stem.

CASE II. A 21 year old white woman was admitted complaining of pain in the right ear and face, associated with numbness of 2 days' duration. The patient was said to have had bulbar poliomyelitis at the age of 16 years. After this illness, the right eighth, ninth, tenth, and eleventh cranial nerves remained weak.

On admission, a dark mass behind the right tympanic membrane and impairment of the right fifth, sixth, seventh, and eighth cranial nerves were noted. The right ninth, tenth, eleventh, and twelfth cranial nerves were completely paralyzed.

Roentgenograms of the skull showed a large area of bone destruction in the area of the right jugular foramen (Fig. 2, *A* and *B*). Selective right and left internal carotid arteriography revealed no abnormality. On vertebral arteriography, the right anterior inferior cerebellar artery was slightly elevated (Fig. 2*C*). In addition, the right posterior inferior cerebellar artery was stretched and displaced to the left of midline. No tumor vessels were noted.

On exploration of the posterior fossa a large tumor was noted in the right cerebellopontine angle. Some areas of the tumor appeared gelatinous, although other areas were of a cartilaginous consistency. Biopsy yielded the pathologic diagnosis of chondroma.

CASE III. A 61 year old white woman was admitted because of hoarseness of 2 months' duration. She had also noted excess salivation and unsteadiness of gait.

On physical examination, left sixth, ninth, tenth, and twelfth cranial nerve palsies were noted. There was complete hearing loss on the left.

Plain skull roentgenograms showed a destructive process involving the floor of the left middle fossa and petrous tip, associated with faint calcification in the parasellar region (Fig.

* From the Department of Radiology, University of California School of Medicine, San Francisco, California.

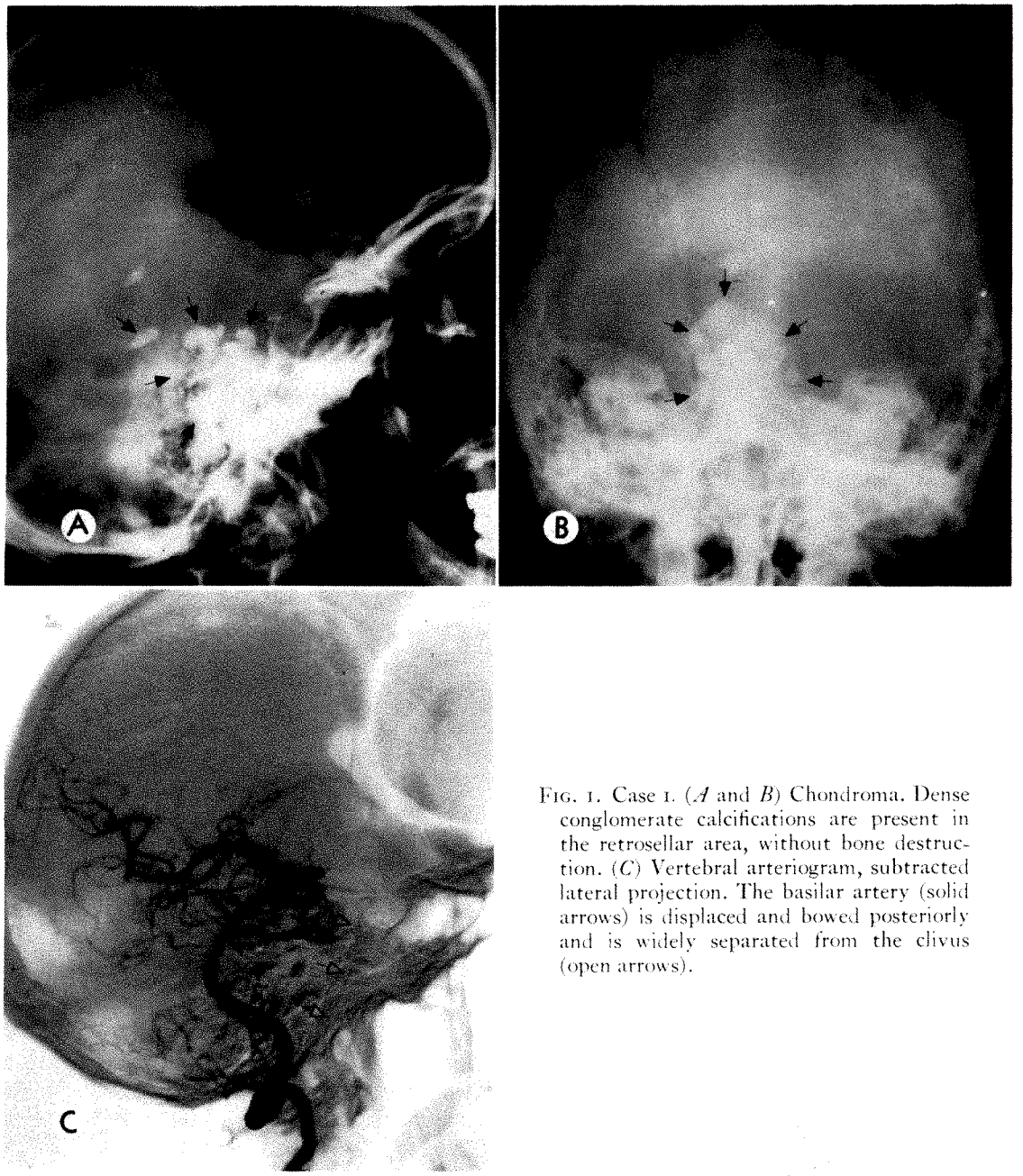


FIG. 1. Case 1. (*A* and *B*) Chondroma. Dense conglomerate calcifications are present in the retrosellar area, without bone destruction. (*C*) Vertebral arteriogram, subtracted lateral projection. The basilar artery (solid arrows) is displaced and bowed posteriorly and is widely separated from the clivus (open arrows).

3, *A* and *B*). Vertebral arteriography showed bowing of the basilar artery to the right. Slight upward and medial displacement of the left posterior cerebral artery was noted. No tumor blush or abnormal vessels were seen.

At surgery, a grayish tumor in the left parasellar region, which involved the floor of the middle fossa and petrous tip, was partially excised. The histologic diagnosis was well differentiated chondrosarcoma. The remaining tumor was then irradiated to a tumor dose of 5,000 r in 48 days.

Symptoms had not progressed when the patient was seen on follow-up examination 13 months later. At that time roentgenograms of the skull showed extensive coarse calcifications

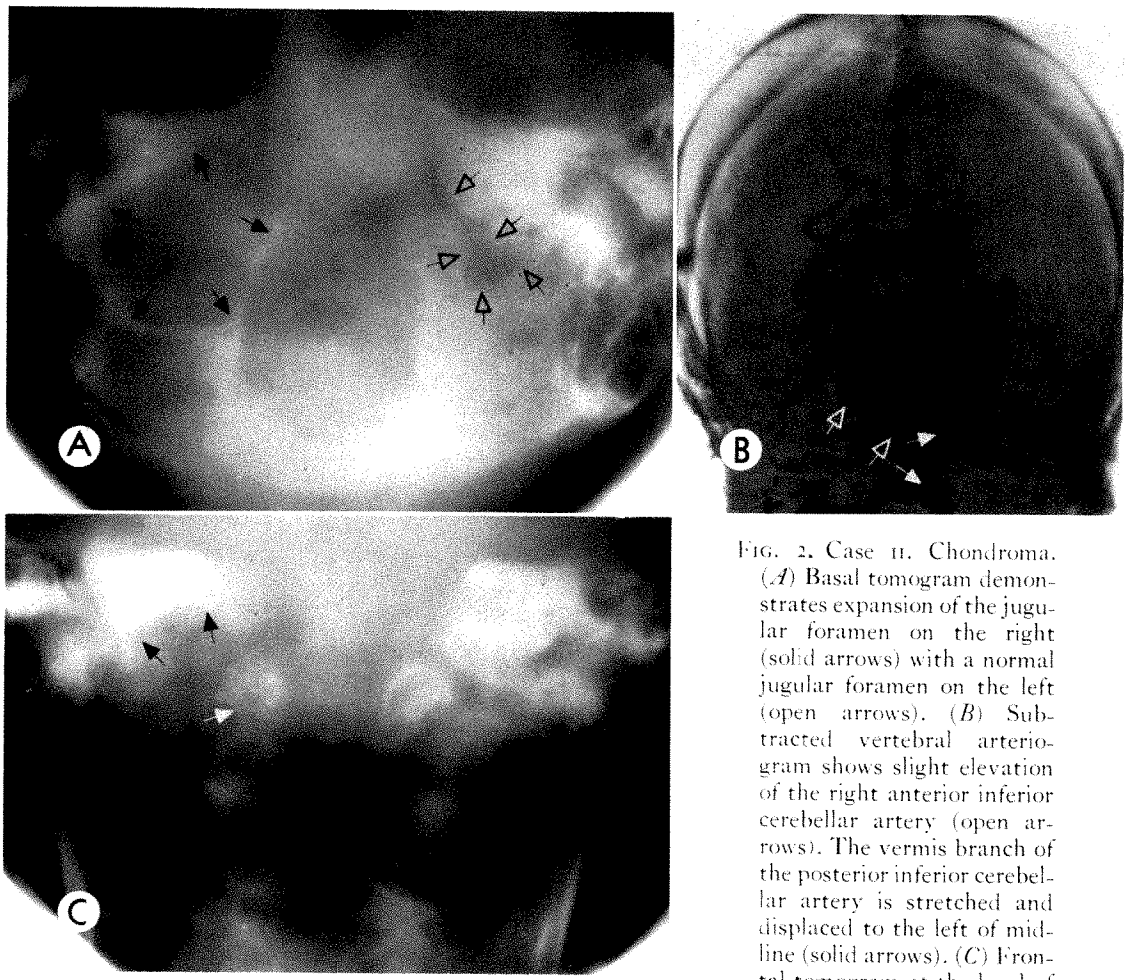


FIG. 2. Case II. Chondroma. (*A*) Basal tomogram demonstrates expansion of the jugular foramen on the right (solid arrows) with a normal jugular foramen on the left (open arrows). (*B*) Subtracted vertebral arteriogram shows slight elevation of the right anterior inferior cerebellar artery (open arrows). The vermis branch of the posterior inferior cerebellar artery is stretched and displaced to the left of midline (solid arrows). (*C*) Frontal tomogram at the level of the internal auditory meatus demonstrates erosion of the inferior aspect of the right petrous tip (black arrows) and erosion of the right occipital condyle (white arrow).

in the left middle fossa (Fig. 3, *C* and *D*). The calcifications were much more pronounced than on the preoperative study.

DISCUSSION

Cartilaginous tumors of the skull base are rare. Leitholf[11] found only 4 chondromas in a series of 4,135 brain tumors. Vandenberg and Coley[17] reviewed 888 malignant and 630 benign primary bone tumors of which only 7 of the malignant and 15 of the benign neoplasms arose from the calvarium. Of these 22, none was a chondroma or chondrosarcoma.

Acquaviva *et al.*[1] found 99 cases of intracranial chondromas reported in the literature and added 2 additional cases. In 66 of these patients, the tumor involved the base of the skull, with the remainder located at various other intracranial sites. No sex predilection had been noted. In the review of Acquaviva *et al.*[1] the sex was noted in 92 patients with intracranial chondromata: 47 men and 45 women. Those tumors located at the skull base, however, showed a slight female preponderance (35 women and 26 men). Cartilaginous tumors of the skull base are noted most commonly between the second and fifth decades.[5] In most instances, they are slowly growing tumors, often with a long history of symptoms as in Cases I and II

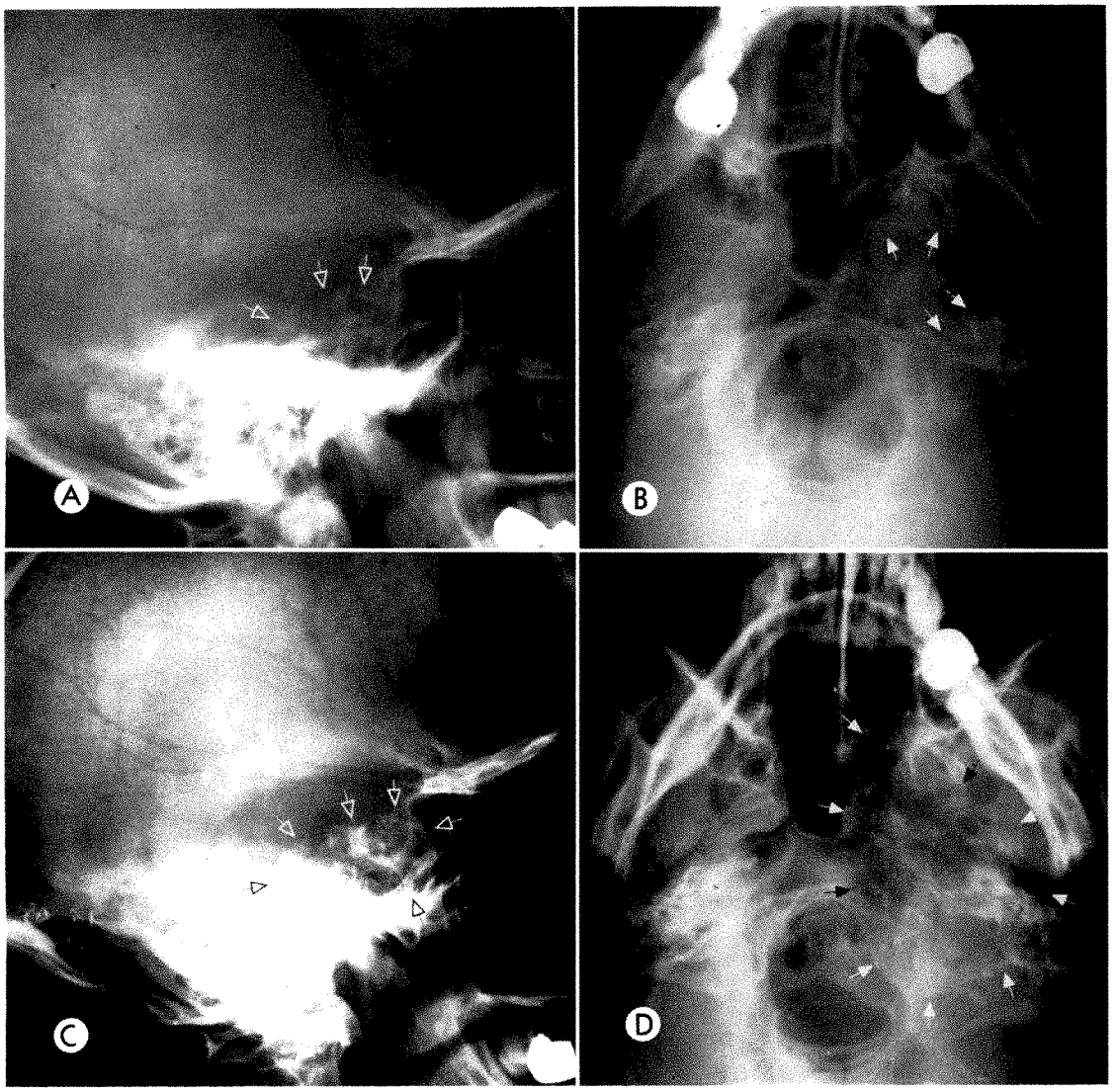


Fig. 3. Case III. Well differentiated chondrosarcoma. (*A*) Faint calcifications are present in the parasellar region. (*B*) Extensive irregular destruction involves the floor of the left middle fossa and apex of the petrous pyramid. (*C* and *D*) Thirteen months after excision and irradiation. Extensive, dense calcification is now present in the left middle fossa. Some reconstitution of the floor of the left middle fossa has taken place.

(15 and 5 years, respectively).

Various classifications of intracranial chondromas have been proposed.[5,8,10] Those tumors arising from the base of the skull comprise a distinct category of intracranial chondromas, according to most authors. Embryologically, the bones of the skull base arise from cartilaginous matrices, as opposed to the cranial vault, which arises from membranous bone. Thus, the predilection of intracranial cartilaginous tumors for the base of the skull is not surprising.[6]

The origin of intracranial chondromas arising from sites other than the base of the skull is somewhat uncertain. Chondromas have been described as arising from such diverse sites as the cranial vault,[13] choroid plexus, dura mater, arachnoid[5] and brain.[8] Chorobski *et al.*[3] have suggested that the source of intracranial chondromas arising from these sites might be embryonal cartilaginous rests.

In patients with Ollier's multiple enchondromatosis, the skull base may occasionally be involved. The osteochondromata associated with multiple osteocartilaginous exostoses, however, apparently do not involve the skull.[9]

ROENTGEN FINDINGS

Of the 53 cartilaginous tumors of the skull base studied with plain roentgenograms in the review by Acquaviva *et al.*,[1] 30 were calcified. The calcification was massive in 13, whereas it was more granular in 17. Tumor calcification was apparent in 2 of our 3 patients (Fig. 1, *A-C*; and 3, *A-D*). In Case I, coarse conglomerates of dense retroclival calcifications were present. The calcifications noted in Case III were of a fainter, more flocculent nature and were parasellar in location. This calcification was noted to be more dense and extensive on re-examination after surgery and irradiation. No calcifications have been reported in chondromas of the cerebellopontine angle.[16] The absence of calcification of the tumor located in the cerebellopontine angle of Case II is, therefore, consistent with the experience of others.[2]

Acquaviva and his associates noted bone destruction in 24 of the 53 patients with chondromas of the skull base. Such destruction was noted in 2 of our patients. A large, sharply defined area of bone destruction in the region of the jugular foramen was noted in Case II. The roentgen and clinical findings suggested the diagnosis of glomus jugulare tumor. This diagnosis was excluded, however, by lack of vascularity on selective internal and external carotid and vertebral arteriography. A more irregular area of extensive destruction was noted along the floor of the left middle fossa and petrous tip in Case III. The appearance simulated that of an invasive nasopharyngeal carcinoma or metastatic neoplasm, but the presence of calcification was against these possibilities.

The review by Acquaviva *et al.*[1] showed that 15 patients with basal cartilaginous tumors had been examined by carotid arteriography. Tumor blush or pathologic vessels were not noted in these patients. Carotid arteriography performed on our Case II demonstrated no abnormality. Vertebral arteriography in all 3 of our patients revealed displaced vessels, but no tumor blush or abnormal vasculature. Vertebral arteriography was performed in Roukkula's 2 patients in whom similar avascular masses were demonstrated.[16]

The patients described in this series illustrate the 3 most common locations of basal cartilaginous tumors: the clivus (Case I), the cerebellopontine angle (Case II), and the parasellar region (Case III). The roentgen and clinical appearances in Case I led to an erroneous preoperative diagnosis of clivus chordoma. The combination of dense retrosellar calcifications with bone destruction has been considered as practically pathognomonic of clivus chordoma.[4] Plaut and Blatt,[14] however, concluded that the differential diagnosis of chondroma and chordoma of the clivus is often difficult and may be impossible. Although the clinical findings associated with chordomas may simulate those of chondromas, the duration of symptoms is usually shorter in chordomas.[12]

Since, to date, no cartilaginous tumors arising in the cerebellopontine angle region have shown calcification, many pathologic conditions must be considered in the differential diagnosis. Acoustic neurinoma, cholesteatoma, meningioma, and glomus jugulare tumors represent some of the more common entities which may simulate chondromas in this region.[7,15] The presence of bone destruction around the right jugular foramen in Case II simulated the appearance of a glomus jugulare tumor.

Chondromas arising in the parasellar area are more likely to be calcified. Fourteen of 16 patients described by Klingler[10] and 5 of 6 patients described by Kleinsasser and Friedmann[9] showed calcifications in parasellar chondromas. In List's series of chondromas of the base of the skull, all 5 parasellar chondromas were calcified.[12] The differential diagnosis of chondromas in this

location, therefore, includes other calcifying parasellar masses, such as aneurysms of the internal carotid artery, meningiomas, craniopharyngiomas, and chordomas.

Arteriography has been a useful procedure, not only for demonstrating the size and location of the tumor, but also in excluding more vascular lesions.

SUMMARY

Intracranial cartilaginous tumors are rare neoplasms, usually arising from the base of the skull.

The clinical and roentgen findings of 3 chondromas arising in this area are reviewed.

The differential diagnoses of these lesions depend primarily on their location.

Bone destruction and calcification are noted frequently on roentgen examination of the skull. Angiography is helpful in demonstrating the size and location of the neoplasm and in showing its avascular nature.

Hideyo Minagi, M.D.
Department of Radiology
University of California
San Francisco Medical Center
San Francisco, California 94122

REFERENCES

1. ACQUAVIVA, R., TAMIC, P. M., THEVENOT, C., FOURNIE, R., GRAU, P., BRU, P., LEBASCLE, J., and ESPLAN, J. F. R. Los condromas intracraneales: revisión de la literatura a propósito de dos casos. *Rev. españ. oto-neuro-oftal.*, 1965, *24*, 15–32.
2. ARONSON, H. A., and OTIS, R. D. Intracranial chondroma involving cerebellopontine angle: report of case. *J. Neurosurg.*, 1962, *19*, 529–531.
3. CHOROBSKI, J., JARZYMSKI, J., and FERENS, E. Intracranial solitary chondroma. *Surg., Gynec. & Obst.*, 1939, *68*, 677–686.
4. DICHIRO, G., and ANDERSON, W. B. Clivus. *Clin. Radiol.*, 1965, *16*, 211–223.
5. FORSYTHE, R. W., BAKER, G. S., DOCKERTY, M. B., and CAMP, J. D. Intracranial osteochondroma. *Proc. Staff Meet. Mayo Clin.*, 1947, *22*, 350–356.
6. GABRIELSEN, T. O., and KINGMAN, A. F., JR. Osteocartilaginous tumors of base of skull: report of unique case and review of literature. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1964, *91*, 1016–1023.
7. HODES, P. J., PENDERGRASS, E. P., and DENNIS, J. M. Cerebellopontine angle tumors: their roentgenologic manifestations. *Radiology*, 1951, *57*, 395–406.
8. KING, L. S., and BUTCHER, J. Osteochondroma of base of skull. *Arch. Path.*, 1944, *37*, 282–285.
9. KLEINSASSER, O., and FRIEDMANN, G. Die Knorpelgeschwülste der Schädelbasis. *Deutsche Ztschr. Nervenh.*, 1958, *177*, 378–404.
10. KLINGLER, M. Über Knorpelgeschwülste der Schädelbasis mit intrakranieller Ausdehnung. *Acta neurochir.*, 1951, *1*, 337–380.
11. LEITHOLF, O. Cited by M. Roukkula.[16]
12. LIST, C. F. Osteochondromas arising from base of skull. *Surg., Gynec. & Obst.*, 1943, *76*, 480–492.
13. MONEY, R. A. Solitary intracranial chondroma. *M. J. Australia*, 1943, *1*, 181–183.
14. PLAUT, H. F., and BLATT, E. S. Chordoma of clivus: report of four cases. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1967, *100*, 639–649.
15. REVILLA, A. G. Differential diagnosis of tumors at cerebellopontine recess. *Bull. Johns Hopkins Hosp.*, 1948, *83*, 187–212.
16. ROUKKULA, M. Roentgenologic findings in chondromas of pontine angle. *Acta radiol.* (Diag.), 1964, *2*, 120–128.
17. VANDENBERG, H. J., JR., and COLEY, B. L. Primary tumors of cranial bones. *Surg., Gynec. & Obst.*, 1950, *90*, 602–612.

THE CALVARIAL "DOUGHNUT LESION": A PREVIOUSLY UNDESCRIBED ENTITY*

By THEODORE E. KEATS, M.D.,† *and* JOHN F. HOLT, M.D.‡
CHARLOTTESVILLE, VIRGINIA AND ANN ARBOR, MICHIGAN

THIS report is concerned with the description and documentation of an innocent but distinctive ring-like lesion of the calvarium which we have designated descriptively as the "calvarial doughnut lesion." The recognition of this lesion as an entity was made by one of us (J.F.H.) 21 years ago, but the lesion has not, as yet, been reported as a distinct entity. Its importance lies in its recognition as a benign process and its differentiation from other lesions with which it may be confused.

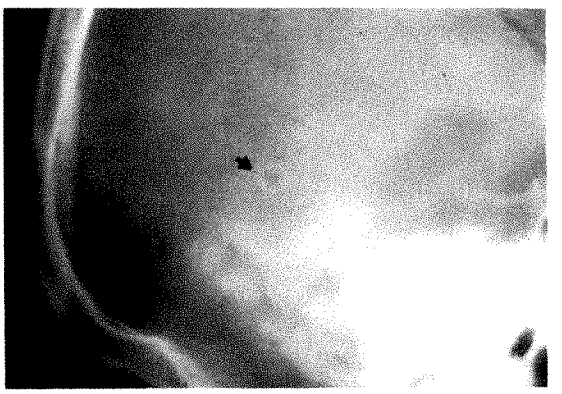


FIG. 1. Lateral projection. A typical Group 1 lesion (arrow) shows a well-defined area of radiolucency surrounded by a dense and well-defined area of sclerotic bone.

REVIEW OF THE LITERATURE

The literature contains a single illustration of a similar lesion. Figure VIII, 5 on page 80 of Middlemiss' book, "Tropical Radiology," illustrates a doughnut lesion in the calvarium of a patient with sickle cell anemia.[1] The lesion is stated to represent an old infarction surrounded by ring calcification. However, correspondence with Dr. Middlemiss and with Dr. W. P. Cockshott, who contributed the chapter in which this illustration is included, indicates that they have no evidence that this lesion does indeed represent an area of infarction other than the fact that it resembles infarcted areas in other bones, nor do they suggest that this lesion is specific for or common in the hemoglobinopathies. Our review of the literature shows no notation of the fact that this lesion may occur spontaneously in otherwise normal skulls.

CLINICAL ASPECTS

One of us (J.F.H.) has recorded 11 of these lesions in the past 21 years and the other (T.E.K.) has collected 13 cases in the past 10 years. This would indicate that this is not a common lesion. Twenty-one of these lesions are illustrated in this report.

The patients in whom these lesions were found ranged in age from 16 to 72 years, the great majority of them occurring in late middle life and in old age.

These lesions were detected, in every case, as an incidental asymptomatic finding, unrelated to the patient's complaint or primary condition. In the 2 patients in whom we have histologic documentation, biopsy was performed on the basis of roentgenographic appearance alone. Unfortunately, we do not have serial roentgenograms on any of these patients and are unable to comment on the evolution of the lesion, but the fact that none of the patients have returned years later with a larger lesion of clinical significance points to the benign nature of the process.

* Presented at the Sixty-ninth Annual Meeting of the American Roentgen Ray Society, New Orleans, Louisiana, October 1–4, 1968.
From the Departments of Radiology, University of Virginia School of Medicine, Charlottesville, Virginia,† and the University of Michigan School of Medicine, Ann Arbor, Michigan.‡

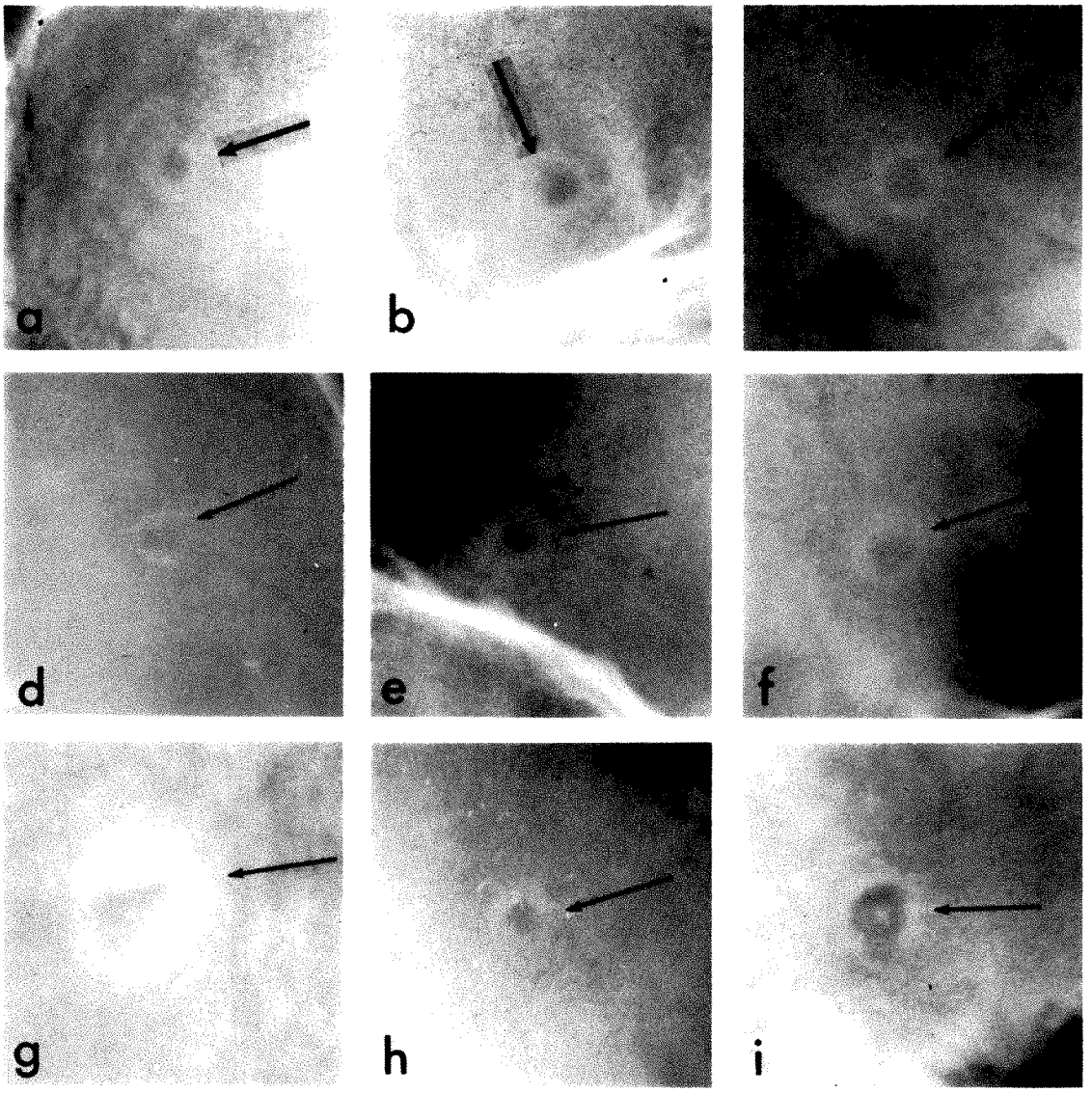


Fig. 2. (*a–i*) Additional Group 1 lesions. (*i*) Note the irregular areas of density of varying size within the central area of radiolucency. (Figure 2*c* courtesy of Dr. O. A. Stienon, Madison, Wisconsin.)

ROENTGEN ASPECTS

The doughnut lesions present a ring-like configuration and may occur in any portion of the calvarium. Their roentgenographic appearance falls into two general groups. The first group presents as a very well-defined area of radiolucency surrounded by a very dense and well-defined area of sclerotic bone (Fig. 1; and 2, *a-i*). In the second group, the lesion tends to be somewhat larger and the radiolucency and the sclerotic margins less regular and less well-defined (Fig. 3; and 4, *a-j*). Lesions of either group may contain irregular areas of density of varying size within the central areas of radiolucency (Fig. 2*i*; 3; and 4, *a*, *g-j*). This feature is more common in the second group of lesions.

PATHOLOGY

We were able to obtain histologic material on 2 patients with doughnut lesions.

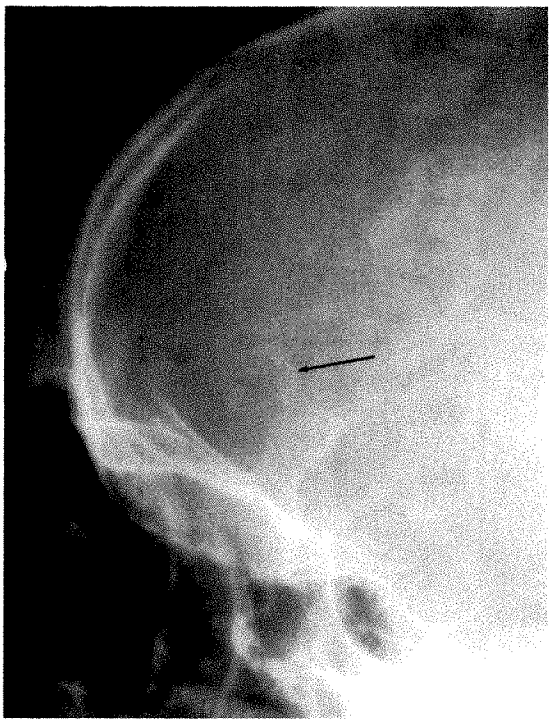


FIG. 3. Lateral projection. A typical Group II lesion (arrow) is larger than the Group I lesion and the radiolucency and the sclerotic margins are less regular and less well-defined.

These are illustrated in Figure 4, *g* and *i*. The microscopic sections available to us incompletely represent the lesion *in toto* due to difficulties in preparation. However, histologic observations on both lesions and information contained in reports by reviewing authorities, who saw a more complete set of slides on one case, indicate some common features: (1) A surrounding ring of sclerotic cortical bone; and (2) a rather sharply defined circular defect within this ring filled with fibrous tissue and containing a nidus of small, irregular bone trabeculae. In one specimen, these trabeculae suggest necrotic bone, but this feature is not described in reports of the other lesions. In the fibrous matrix of the former lesion there are also collections of foamy macrophages with a slight brown pigment, but no signs of osteoblastic or osteoclastic proliferation or hemosiderin deposition. The cellular detail of the other specimen does not permit recognition of this element.

This entity appears to represent a lesion of reactive fibrosis to injury. This would be consistent with a bone infarction, but several other suggestions of benign reparative lesions were advanced by other authorities.

COMMENT

This lesion appears to represent a distinct entity. Its similarity to the lesions of bone infarction found elsewhere in the skeleton and its predominant occurrence late in life tend to suggest a similar etiology. The histologic appearance based on two specimens is compatible with the changes one might anticipate in such an event, considering that these occur in membranous rather than chondromatous bone where the recognized pattern of callus proliferation is dissimilar.

The importance of the recognition of a doughnut lesion is only that it not be confused with clinically significant lesions. Two such entities with which it might be confused are the intradiploic epidermoid and the eosinophilic granuloma, but both are readily distinguishable. The intradiploic epidermoid usually presents as a round area of radiolucency with a well-defined, sharply outlined thin border of sclerosis. No central area of density is seen. The eosinophilic granuloma may have a central sequestrum but is not marginated by sclerotic bone. In addition, both of these lesions are symptomatic which, in turn, leads to their discovery. The possibility that these lesions represent regressing areas of eosinophilic granuloma is most unlikely, since, with rare exception, these heal without sclerosis and, in addition, have much more irregular contours than do the doughnut lesions.

A fruitful area for further investigation of this problem is the study of the doughnut lesion over a long period of time in an attempt to learn more of its natural history. It is entirely possible that the spectrum of roentgenographic appearances seen in the cases presented here represent stages in the evolution of this lesion with

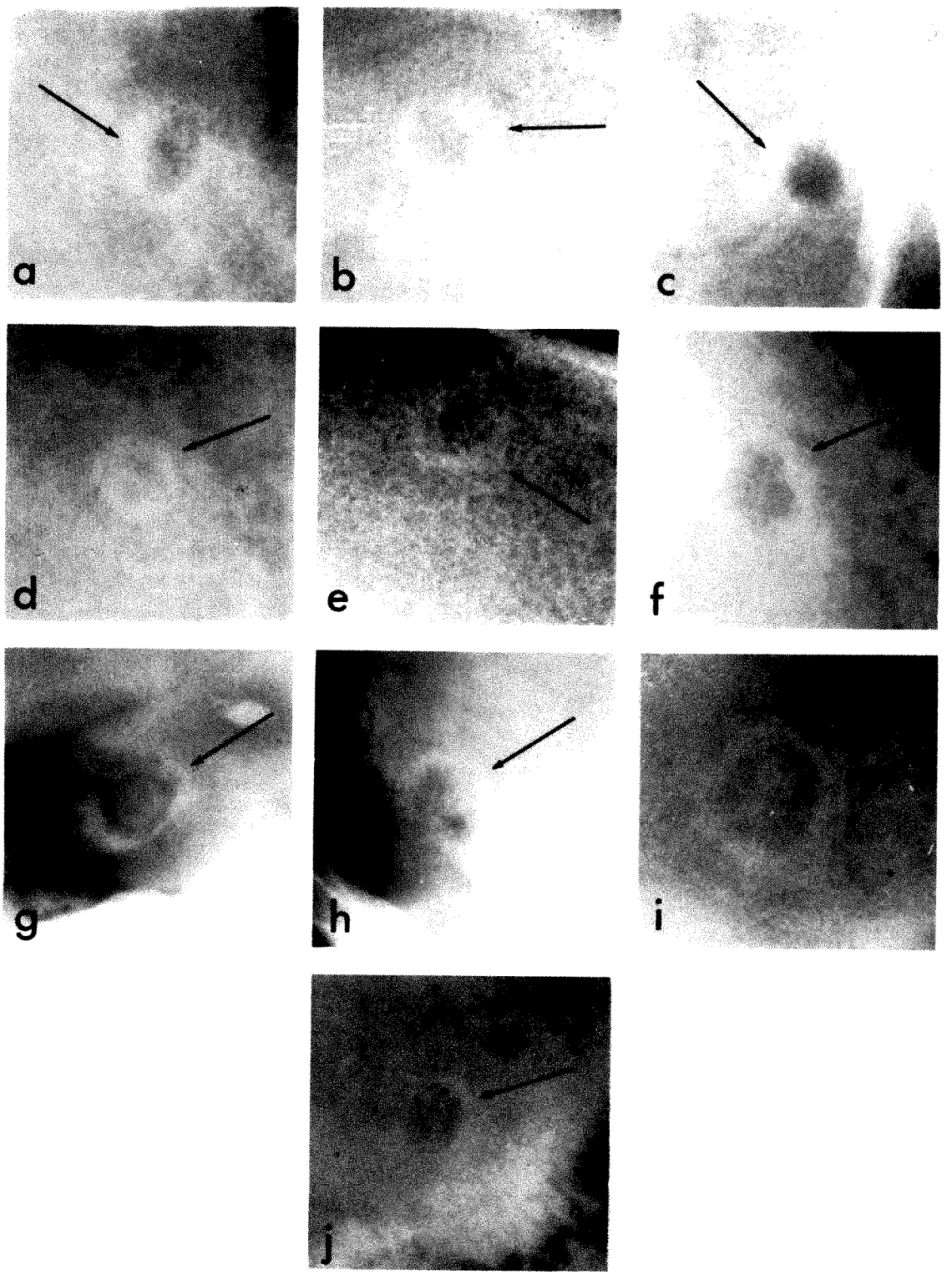


Fig. 4. (*a–j*) Additional Group II lesions. (*a, g–j*) A more common feature in this group are the irregular areas of density of varying size within the central areas of radiolucency.

the smaller, well-defined, thick-walled type representing an end stage.

SUMMARY

A benign asymptomatic ring-like lesion of the calvarium, which has been termed the "doughnut lesion," has been described. This lesion is discovered as an incidental finding. The importance of its recognition lies only in its distinction from significant calvarial lesions with which it may be confused.

Theodore E. Keats, M.D.
Department of Radiology
University of Virginia School of Medicine
Charlottesville, Virginia 22901

The authors wish to express their appreciation to Dr. Allen E. Green of Memphis, Tennessee for the roentgenographic and histologic material of the patient illustrated in Figure 4g, to the Departments of Radiology and Pathology of the University of Missouri School of Medicine for use of the roentgenographic and histologic material collected while one of us (T.E.K.) was a member of that faculty, and to the Department of Pathology, University of Virginia School of Medicine for their assistance in the analysis of the histologic material.

REFERENCE

1. MIDDLEMISS, H. Tropical Radiology. William Heinemann, Ltd., London, 1961.

VOL. 105, NO. 2

CALVARIAL BONE DEFECTS IN NEUROFIBROMATOSIS*

A CASE REPORT

By M. M. SAHA,† K. N. AGARWAL,‡ *and* O. P. BHARDWAJ†
NEW DELHI, INDIA

OCCURRENCE of osteolytic lesions in the skull in neurofibromatosis is rare and involvement of the right lambdoid suture is almost unknown. Neurofibromatosis classically exhibits multiple cutaneous nodules (fibroma molluscum), cutaneous pigmentation (café au lait spots) and neurofibromas of peripheral nerves. The systemic manifestations and roentgenologic abnormalities have been reviewed in detail by Hunt and Pugh[2] and Meszaros *et al.*[4] In their review of 192 cases of neurofibromatosis, Hunt and Pugh[2] mentioned 3 cases of small defects in the calvarium. In another case there was evidence of cranium bifidum. Joffe[3] described 4 cases of neurofibromatosis with calvarial bone defects involving the lambdoid suture on the left side. Davidson[1] reported 6 cases of neurofibromatosis, of which 3 cases showed osteolytic lesions in the skull and involvement of the left lambdoid suture.

The purpose of this paper is to report a case of neurofibromatosis with multiple osteolytic skull defects sparing the left lambdoid suture. There was, however, involvement of the right lambdoid suture.

REPORT OF A CASE

U.D., a 16 year old female was admitted to Irwin Hospital with a 10 month history of gradually developing small, multiple, non-tender cutaneous nodules covering the entire body. She also complained of feeling some soft areas in the skull on the posterior aspect.

Other members of the family did not show evidence of neurofibromatosis.

On physical examination, there were multiple pigmented spots and nodules of the skin.

There were two soft tender areas surrounded by a thick bone margin in the right post-auricular and occipital regions (7×2.5 cm. and 3.0×1.0 cm., respectively). There were no cutaneous nodules overlying these soft areas. On the skull there was one cutaneous nodular swelling 1.0 cm. in diameter in the left temporal region. Other systemic examinations were essentially normal. Laboratory studies showed hemoglobin 13.0 gm. per cent, leukocyte count 8,600/cu. mm., peripheral smear and bone marrow normal, serum cholesterol 100 mg. per cent, and urine and fundi normal.

Roentgen Findings. Roentgenograms of the skull showed multiple well-defined osteolytic areas mainly in the occipital and posterior part of the parietal bones. One of the osteolytic areas involved the right lambdoid suture, while the left one was not affected (Fig. 1; 2;

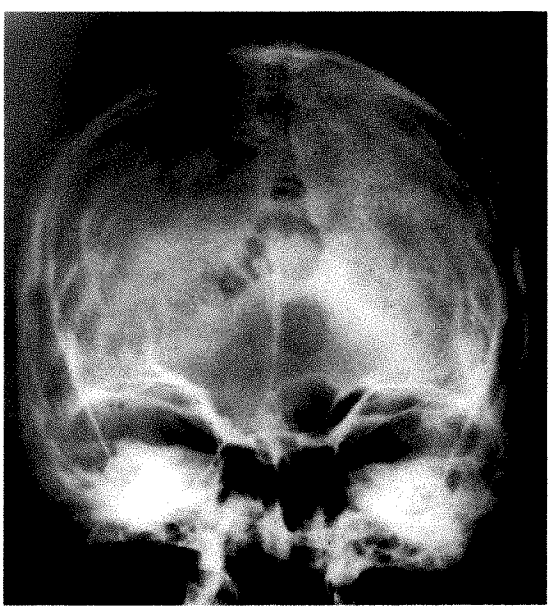


FIG. 1. Anteroposterior view of the skull shows well-defined osteolytic areas in the occipital and parietal bones adjoining the lambdoid suture. One of the osteolytic areas shows involvement of the right lambdoid suture.

* From the Department of Radiology† and Haematology Unit, Department of Pediatrics, ‡ the Maulana Azad Medical College and Associated Irwin and G. B. Pant Hospitals, New Delhi, India.

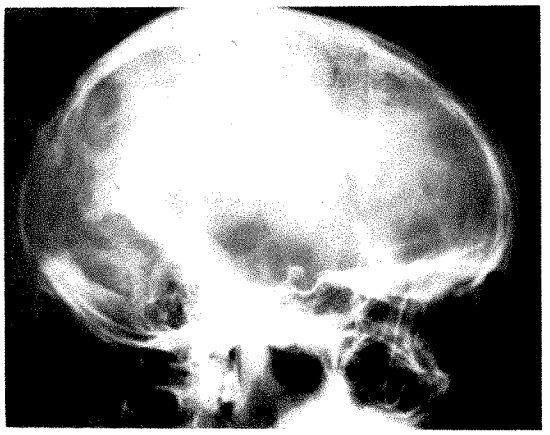


FIG. 2. Lateral view of the skull shows the osteolytic areas confined to the occipital and posterior part of the parietal bones.

and 3). The right mastoid was poorly pneumatized, but the left side showed normal pneumatization (Fig. 3). In the spine there was mild scoliosis of the lumbodorsal region. The pedicles of D_{12}, L_1 and L_2 vertebrae showed thinning on the left side. The left twelfth rib and the left transverse processes of L_1 and L_2 vertebrae also showed thinning (Fig. 4). The remaining skeleton demonstrated no abnormality. Myelography was normal. The skeletal changes were thought to be due either to neurofibromatosis or histiocytosis.

DISCUSSION

The bone defects in neurofibromatosis may be caused by overlying neurofibromata, but cases have been reported where there was no evidence of neurofibroma overlying the bone defect. Furthermore, histopathologic studies of the tissues from the osteolytic areas in some cases of neurofibromatosis showed no evidence of neurofibromatous tissue. On this basis, Hunt and Pugh[2] suggested that in addition to neuroectodermal dysplasia, there is also mesodermal dysplasia present. In our case, biopsy taken from the bony margin of the osteolytic area revealed evidence of neurofibromatosis, although there was no neurofibromatous nodule overlying the osteolytic area.

In all 4 cases described by Joffe,[3] there

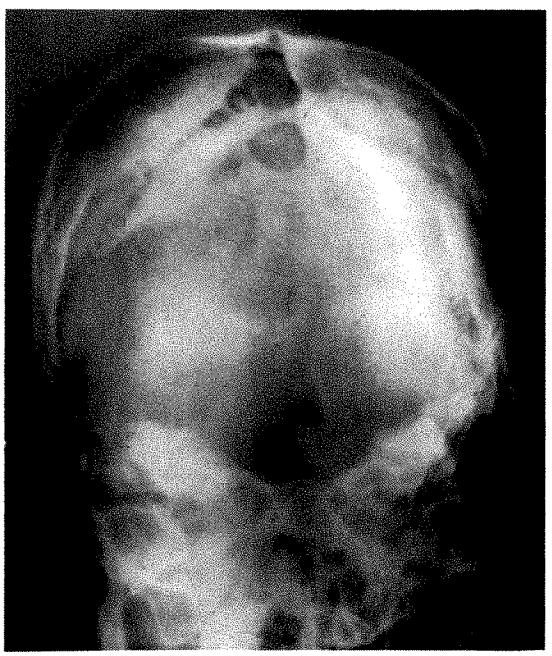


FIG. 3. Towne's view of skull shows poor pneumatization of the right mastoid. Left mastoid shows normal pneumatization. Involvement of the right lambdoid suture is also seen.

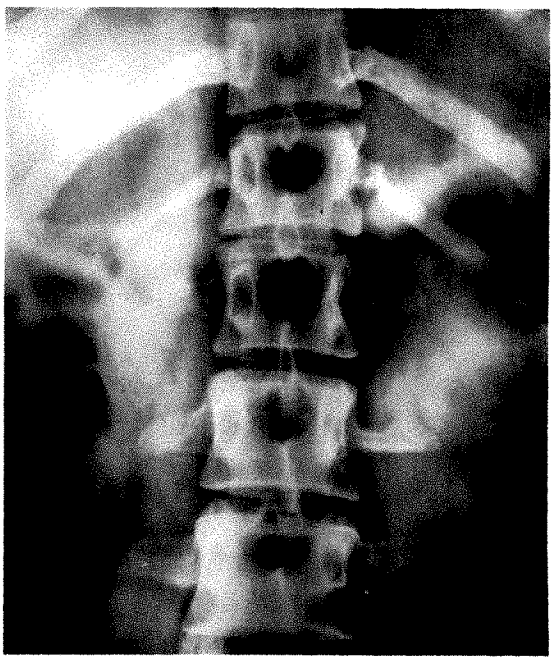


FIG. 4. Anteroposterior view of lumbodorsal spine shows mild scoliosis and thinning of pedicles of D_{12}, L_1 and L_2 vertebrae on the left side. Left twelfth rib and left transverse processes of L_1 and L_2 vertebrae also show thinning.

was involvement of the lambdoid suture on the left side. In addition, there was also associated poor or absent pneumatization of the corresponding mastoid in all cases. Davidson's 3 cases, reported later, also showed involvement of the left lambdoid suture. However, he did not comment upon the pneumatization of the mastoids.

In contrast to involvement of the left lambdoid suture in the 7 cases of Joffe[3] and Davidson,[1] the present case showed involvement of the right lambdoid suture. There was poor pneumatization of the corresponding mastoid in this case, as was also observed by Joffe.[3]

SUMMARY

A rare case of neurofibromatosis with calvarial bone defects is reported. There was involvement of the right lambdoid suture which has not been previously mentioned in the radiologic literature. There was also poor pneumatization of the right mastoid.

M. M. Saha, M.D.
Department of Radiology
Maulana Azad Medical College and Associated Irwin and G. B. Pant Hospitals
New Delhi-1
India

REFERENCES

1. DAVIDSON, K. C. Cranial and intracranial lesions in neurofibromatosis. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1966, *98*, 550–556.
2. HUNT, J. C., and PUGH, D. G. Skeletal lesions in neurofibromatosis. *Radiology*, 1961, *76*, 1–20.
3. JOFFE, N. Calvarial bone defects involving lambdoid suture in neurofibromatosis. *Brit. J. Radiol.*, 1965, *38*, 23–27.
4. MESZAROS, W. T., GUZZO, F., and SCHORSCH, H. Neurofibromatosis. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1966, *98*, 557–569.

SARCOIDOSIS OF THE SKULL*

REPORT OF A CASE

By OSCAR A. TURNER, M.D.,† *and* SANFORD R. WEISS, M.D.‡
YOUNGSTOWN, OHIO

ALTHOUGH secondary invasion and destruction of the bones of the skull may occur occasionally from sarcoid involving contiguous structures, independent involvement of the calvarium is quite rare, particularly in view of the frequency of the disease elsewhere in the body. A search of the literature disclosed only 4 cases, 3 of which were documented in detail (Table 1). In these 3 cases there were several systems involved and all showed evidence of chronic or extensive sarcoidosis and skull lesions which were multiple. The present case is one in which the diagnosis of sarcoid involvement of the skull was suspected because of the roentgenologic appearance of the skull lesion and the roentgenographic findings in the chest, but in which the diagnosis was established definitely only after removal and examination of the area of involvement in the calvarium.

REPORT OF A CASE

The patient was a 34 year old, white male admitted to the North Unit of The Youngstown Hospital Association on December 12, 1967, for evaluation and treatment because of the presence of a small swelling in the left parieto-occipital region, associated with an underlying lytic area in the skull. Prior to admission he worked as a helper in a grocery store and in the course of work bumped his head against a car trunk lid in November of 1967. Despite the fact that the injury was of a minor nature, local soreness and pain persisted and became more severe with the development of an area of swelling and tumefaction occurring about 3–4 weeks after injury. He was seen by a general surgeon about 1 week after the appearance of the swelling. The tumefaction was aspirated, obtaining a small amount of brown, purulent appearing material, which histologically contained leukocytes and tissue debris but no organisms on smear or culture. Roentgen-

TABLE I

SUMMARY OF REPORTED CASES OF CRANIAL SARCOIDOSIS

Case No.	Reference	Age Sex	Location of Skull Lesions	Other Bone Lesions	Central Nervous System Lesions	Cutaneous Lesions	Other Regions Involved	Confirmation of Skull Lesion	Roentgenologic and Other Information
1	Nielsen[1]	—	Frontal					Biopsy	No evidence of periosteal reaction of sequestration roentgenologically
2	Olsen[2]	51	Left parietal and frontal. Multiple lesions, 0.2–3.0 cm. diameter	None	None	Vulva	Cervical lymph nodes	Biopsy of cervical lymph nodes, skull and vulva	Chest roentgenogram and sternal bone marrow biopsy normal. Multiple areas of bone destruction, well demarcated. No surrounding reactive or sclerotic change
3	Posner[3]	28 mo. F	Multiple small areas without involvement of diploe	Long bones Marrow	About pituitary capsule	None	Lungs, kidneys, liver, spleen, diffuse lymph node involvement	Autopsy	Multiple small areas of porosity without periosteal reaction. Bone formation prominent microscopically
4	Tierstein *et al.*[4]	38 F	3 lesions in frontal area, bilateral	None	None	Scapular and left deltoid area	Parotid. Orbital mass, first on left then on right. Lacrimal gland	2 years after appearance	Destructive lesion of bone, well demarcated but ragged. No bone reaction

* From the Division of Neurological Surgery,† and the Department of Radiology,‡ The Youngstown Hospital Association, North Unit, Youngstown, Ohio.

ograms obtained at this time disclosed the lytic lesion, resulting in his referral and admittance to the Neurosurgical Service.

Neurologic examination revealed no abnormality except for a limited intellectual capacity and the presence of a 2×2 cm., soft, moderately tender swelling in the left parieto-occipital area. There were no signs of inflammation, no evidence of lymphadenopathy and a general medical examination was essentially normal.

Roentgenograms of the chest disclosed nodular infiltration, scattered diffusely throughout both lung fields with no indication of enlarged hilar or mediastinal lymph nodes. These changes were interpreted as being most compatible with pulmonary sarcoidosis; however, other types of chronic granulomatous processes, or metastatic malignancy could not be excluded (Fig. 1). Roentgenograms of the skull revealed a lytic lesion in the left posterior parietal area, measuring 7×17 mm. in diameter (Fig. 2*A*). The bone defect was fairly well circumscribed but slightly irregular in outline with no sclerotic border: no evidence of periosteal reaction was present. There was destruction of the diploic space and both the inner and outer tables of the skull (Fig. 2*B*). Roentgenograms of the

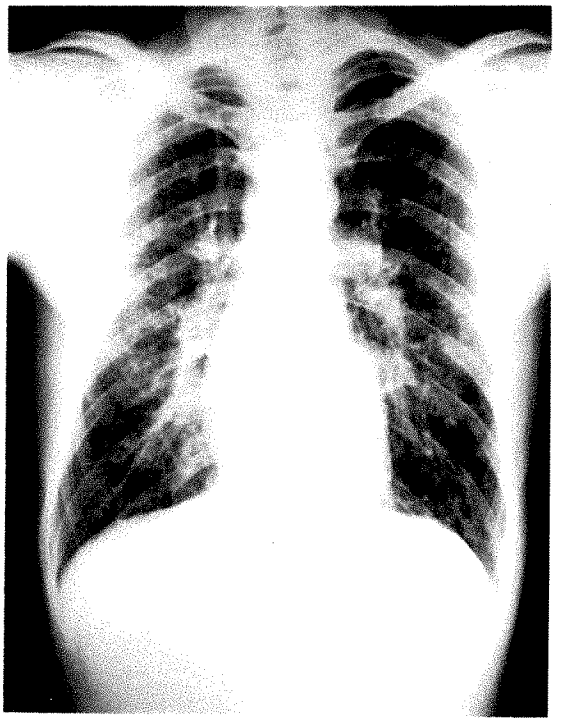


Fig. 1. Roentgenogram of the chest showing bilateral nodular infiltration.

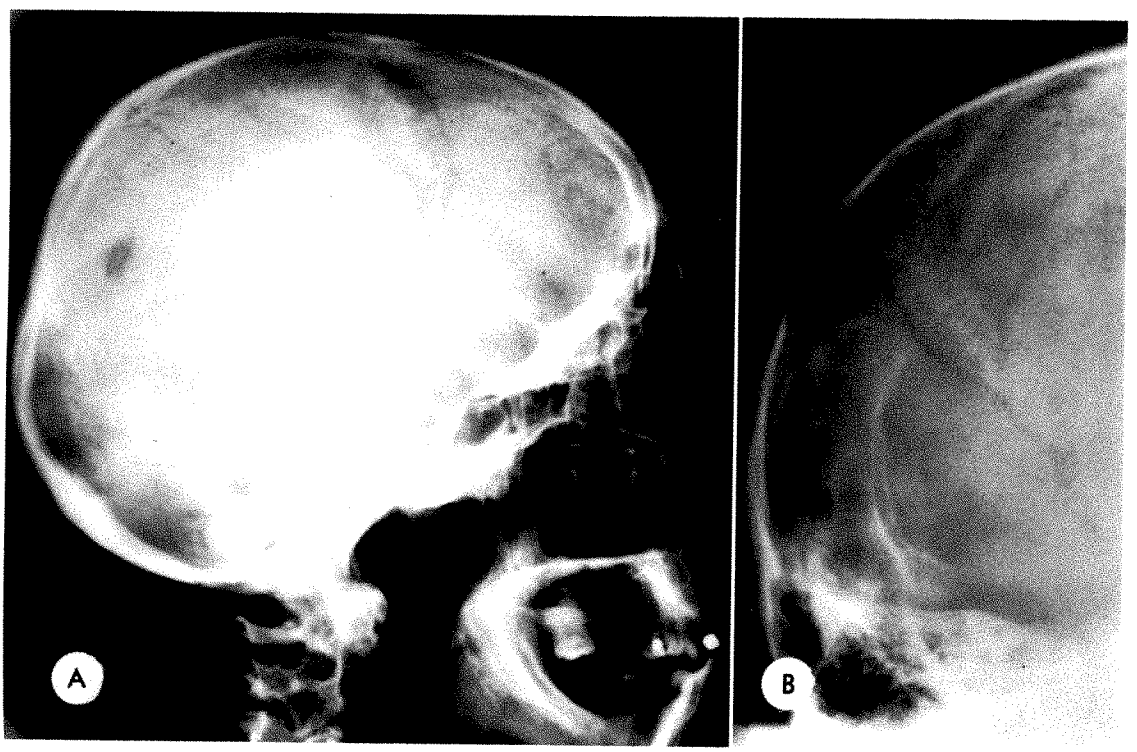


Fig. 2. (*A*) Roentgenogram of the skull showing the well-defined but irregular lytic defect. (*B*) Tangential roentgenogram of lytic lesion showing destruction of both tables and the absence of bone reaction.

lumbosacral spine, pelvis, hands and feet were normal. No abnormality was found in the blood cell count, urinalysis, or spinal fluid studies. The electrophoretic determination of albumin, globulin and A/G ratio were not unusual. Skin tests for histoplasmosis and coccidiosis were negative. Brain scanning with technetium 99m disclosed an area of increased uptake at the site of the lesion, this appearing peripherally located with no evidence of involvement of the brain.

The area was biopsied and a small amount of tissue removed from beneath the scalp. The tissue was grayish-yellow, friable and tended to infiltrate the pericranium but no attempt was made to biopsy the involved bone. There was a defect of the outer table, measuring 0.5 cm. in diameter, when exposed. Microscopically the tissue was composed of fibroblastic cells with scattered lymphocytes, a few giant cells and very occasional epithelioid cells. The tissue was interpreted as a possible fibroblastic meningioma. Left carotid arteriography revealed no abnormalities and, accordingly, a total excision of the lesion was performed with removal of a 5 cm., circular segment of bone. Reflection of the scalp disclosed only a few small areas in which abnormal tissue could be recognized but the underside of the bone flap was covered centrally by adherent and infiltrating granulomatous tissue over an area measuring 3×2 cm. This tissue had infiltrated the outer leaf of the dura as well, and after removal of this area of the dura it could be seen that the granulation tissue, which was 0.5 cm. thick at its maximum, had not penetrated the dura and had not involved the underlying brain. A synthetic dural graft was used and a tantalum cranioplasty done to repair the defect.

Microscopic examination of the area of dural implant revealed an inflammatory infiltrate, consisting mostly of mononuclear cells with numerous lymphocytes and histiocytes. Within the inflammatory area were foci of epithelioid cells, containing an abundant amount of eosinophilic cytoplasm (Fig. 3*A*). These areas showed no evidence of caseous necrosis. Occasional multinucleated cells were also present. Microscopically only the outer half of the dural membrane was involved. Sections of the bone showed diffuse infiltration by inflammatory cells and epithelioid granulomas with occasional delicate spicules of osseous tissue trapped within the inflammatory mass. While the cortical bone was rather dense at the periphery, no actual sclerosis was evident (Fig. 3*B*). Acid fast stains and stains for fungi revealed no organisms.

DISCUSSION

The relationship of the local trauma to the skull lesion in this case is not clear. At the time of biopsy the overgrowth of fibroblastic tissue resembled meningioma and because of the short interval between the trauma and the appearance of the growth, there was thought to be no relationship. However, after the diagnosis of sarcoidosis of the skull was established at

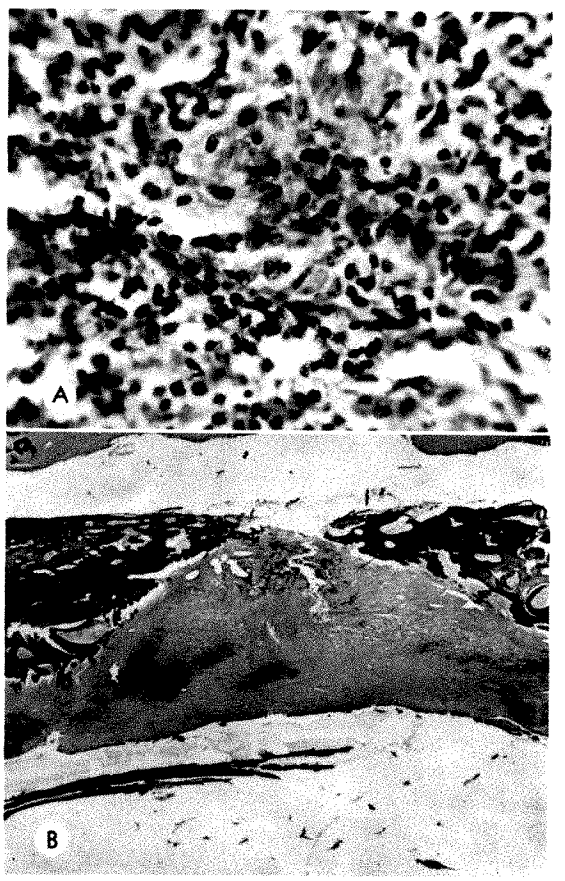


FIG. 3. (*A*) Photomicrograph of the granuloma. Note the nest of epitheloid cells in the surrounding inflammatory tissue. (H. & E.; magnification approximately 500×.) (*B*) Photomicrograph of decalcified section of involved area of the skull. Note absence of sclerosis of bone and destruction of both tables. (H. & E.; magnification approximately 50×.)

the time of excision of the lesion, the possibility of the trauma being an initiating factor became more conceivable. In none of the previously reported 4 cases was there any associated trauma.

This case also differs from the others in that there was a single lesion in the skull. In all of the reported cases, the present one included, there was evidence of sarcoidosis elsewhere in the body. Only in the present instance, however, was there destruction of both the inner and outer tables of the skull. In all cases the area of bone involvement was purely lytic, with no evidence of periosteal reaction or sclerosis surrounding the defect. When the lesion is single, as in this case, the most important differential diagnosis would include that of eosinophilic granuloma and osteolytic response to a meningioma. When there are multiple areas of involvement, multiple myeloma and osteolytic response to metastases must be considered.

Although sarcoidosis is a multi-system disease, involvement of the skeletal system is now recognized as occurring much less frequently than originally thought and when it does occur is usually limited to the hands and feet. Although sarcoidosis of the skull is one of the least frequently seen manifestations of this disease, it should certainly be an important consideration when single or multiple lytic areas are seen in the skull in association with evidence of sarcoidosis elsewhere.

SUMMARY

A case is reported of a 34 year old male in whom a single destructive lesion of the skull due to sarcoidosis developed following minor trauma.

This patient had pulmonary sarcoidosis on roentgenography and represents the fifth case of cranial sarcoidosis reported in the literature.

Oscar A. Turner, M.D.
2136 Glenwood Avenue
Youngstown, Ohio 44511

REFERENCES

1. Nielsen, J. Recherches radiologiques sur les lésions des os et des poumons dans les sarcoïdes de Boeck. *Bull. Soc. Franç. dermat. et syph.*, 1934, *41*, 1187–1218.
2. Olsen, T. G. Sarcoidosis of skull. *Radiology*, 1963, *80*, 232–235.
3. Posner, I. Sarcoidosis: case report. *J. Pediat.*, 1942, *20*, 486–495.
4. Tierstein, A. S., Wolf, B. S., and Siltzbach, L. E. Sarcoidosis of skull. *New England J. Med.*, 1961, *265*, 65–68.

AN UNUSUAL ANGIOGRAPHIC APPEARANCE OF CEREBRAL ARTERIOVENOUS MALFORMATIONS*

By LTC WILLIAM M. HAMMON, MC, USA
WASHINGTON, D. C.

CEREBRAL arteriovenous malformations frequently become clinically manifest as the result of an intracranial hemorrhage. The bleeding may occur only into the subarachnoid space or into a ventricular cavity, but is more frequently associated with an intracerebral hematoma. Usually, the intracranial hemorrhage associated with arteriovenous malformations is less lethal than that associated with bleeding arterial aneurysms, but is more frequently associated with a localized intracerebral hematoma.

There is no doubt that the therapy of choice for all clinically and roentgenologically confirmed cerebral arteriovenous malformations that have hemorrhaged is surgical excision of the entire lesion and evacuation of any associated hematoma.

Cerebral angiography is usually successful in demonstrating the malformation. It aids also in eliminating from serious consideration other causes of hemorrhage and/or space-occupying masses. The two most frequently encountered and easily identified types of arteriovenous malformations are shown in Figures 1 and 2.

Two unusual cases of histologically verified arteriovenous malformations have been seen and treated by the author. To our knowledge a similar angiographic pattern has not been previously reported in the literature.[1–10]

REPORT OF CASES

CASE 1. W. D. was a 7 year old Caucasian who, for 2 weeks prior to admission to the U. S. Army Hospital, Frankfurt, Germany, complained of headache, tiredness and occasional vomiting. Two days prior to admission he fell at school and reportedly hit his head and was admitted to the hospital on February 3, 1966 for observation because of severe headache and vomiting.

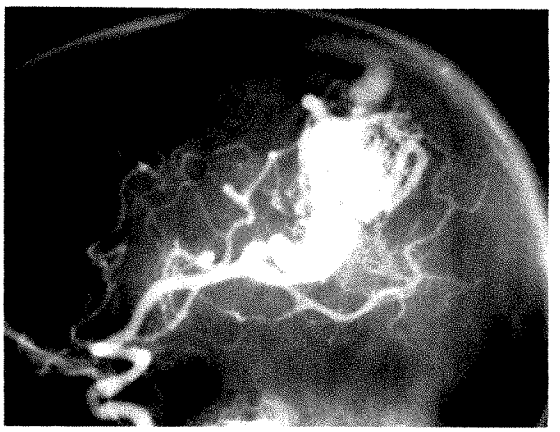


FIG. 1. Typical large convexity arteriovenous malformation.

Physical examination on admission revealed a crying child complaining only of headache. No abnormal general physical or neurologic findings were noted except a pulse rate of 70–80 per minute.

Significant laboratory studies on admission revealed a peripheral white blood cell count of 16,000 with 79 per cent neutrophils. Urinalysis revealed a 2+ sugar, 4+ acetone, negative protein and a normal microscopic examination.

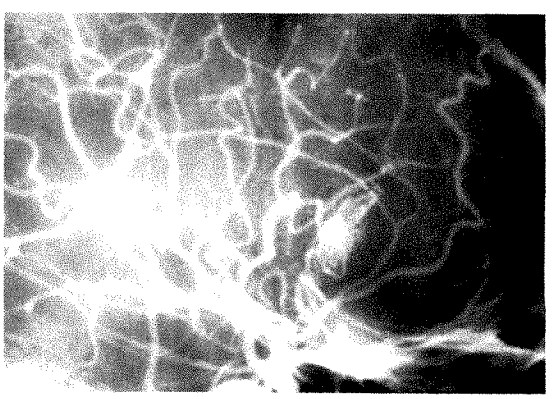


FIG. 2. Typical small arteriovenous malformation with associated intracerebral hematoma, anteroinferiorly.

* From the Neurosurgery Service, Walter Reed General Hospital, Washington, D. C.

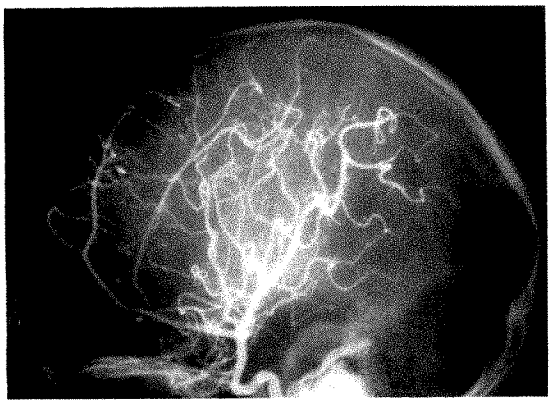


Fig. 3. Case 1. Left lateral arterial phase with abnormal anterior cerebral-callosal marginal artery.

Cerebrospinal fluid examination showed grossly bloody fluid in 3 tubes with 200 white blood cells (80 per cent lymphocytes) per mm.^{3}, 10,000 red blood cells per mm.^{3} without crenation and without xanthochromia. Spinal fluid sugar was 122 mg. per cent and total protein was 362 mg. per cent. Skull roentgenograms were normal. Repeat urinalysis the day following admission was normal.

Course in the Hospital. The patient was evaluated initially for a head injury until the history preceding the schoolyard accident was obtained. The headache persisted and the patient remained in bed due to severe head pain on movement. Four days after admission the patient showed the first evidence of papilledema. An electroencephalogram showed suggestive evidence of increased intracranial pressure and left-sided suppression. The bradycardia persisted. Five days after admission

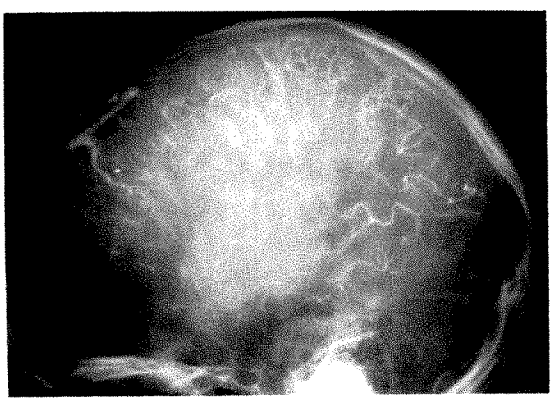


Fig. 4. Case 1. Left lateral late arterial phase with early venous drainage from the abnormal area.



Fig. 5. Case 1. Arterial phase, half-axial projection, with anterior cerebral artery shift and abnormal vasculature.

carotid angiography was performed which demonstrated a large left frontal lobe mass with "tumor" vessels and early venous drainage (Fig. 3, 4, 5 and 6). An intrinsic frontal lobe neoplasm was suspected. Corticosteroid medication was begun and 7 days after admission a left frontal craniotomy was performed; a left frontal lobe hematoma was encountered which had entered the frontal horn of the left lateral ventricle. The hematoma was removed and no neoplasm was seen. Multiple biopsies were taken from the hematoma walls and submitted for histologic examination as well as the non-liquid portions of the hematoma. No



Fig. 6. Case 1. Late arterial, early capillary phase with early venous drainage from abnormal area.

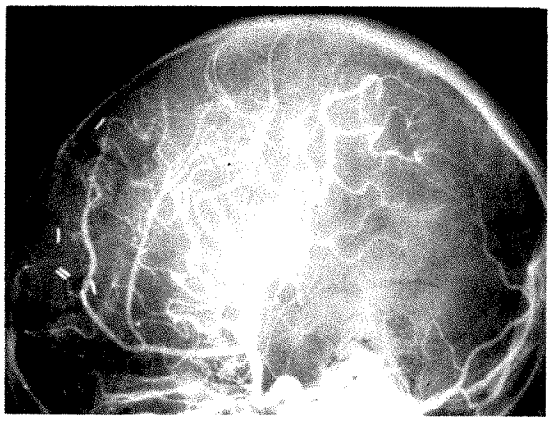


FIG. 7. Case I. Postoperative lateral arterial phase. Abnormal callosal-marginal artery remains.

tumor was seen in the pathologic specimens but an arteriovenous anomaly was noted.

The patient had a rapid and full recovery and was discharged home 7 days following surgery. He was then re-admitted for postoperative angiography 4 weeks later. Evidence of the space-occupying mass was no longer present, but the abnormal vascular pattern associated with the left callosal marginal artery was again noted, as well as the early venous drainage from this region (Fig. 7 and 8). It was decided to perform no further surgery at that time. An underlying neoplasm was still foremost in the author's differential diagnosis, even though pathologic review confirmed the presence of the arteriovenous malformation.

It is now over 2 years since the boy had surgery and he is perfectly normal and well. A technetium brain scan performed recently was normal.



FIG. 8. Case I. Postoperative angiographic Towne projection, arterial phase. Hematoma evacuated, no anterior cerebral shift.

CASE II. J. B. was a 21 year old Caucasian soldier who was admitted to a referring hospital on March 27, 1967 with signs and symptoms of an upper respiratory tract infection. His fever was gone the day after admission but he then developed nausea, vomiting, lethargy, and confusion. A lumbar puncture revealed bloody fluid. A repeat lumbar puncture the next day revealed gross blood again with xanthochromia, a total protein of 240 mg. per cent, and 1,500 white blood cells (82 per cent neutrophils). He then developed an extensor toe sign on the left, became more somnolent and was transferred to Walter Reed General Hospital on April 1, 1967 with the diagnosis of subarachnoid hemorrhage.

Physical examination on admission revealed an afebrile man with normal vital signs but who was lethargic, yet oriented. He had moderate nuchal rigidity, no papilledema and an otherwise normal general physical and neurologic examination, except for unsustained left ankle clonus and a left extensor toe sign.

Laboratory data were all essentially normal, as were the skull roentgenograms. On April 4, the patient had carotid angiography performed, which revealed a large vascular tumor mass in the anterior right frontal lobe with abnormal feeding arteries and early venous drainage (Fig. 9, 10 and 11). This study was interpreted as consistent with a malignant intrinsic right frontal lobe tumor, with a dural vascular response as well.

Course in the Hospital. After appropriate

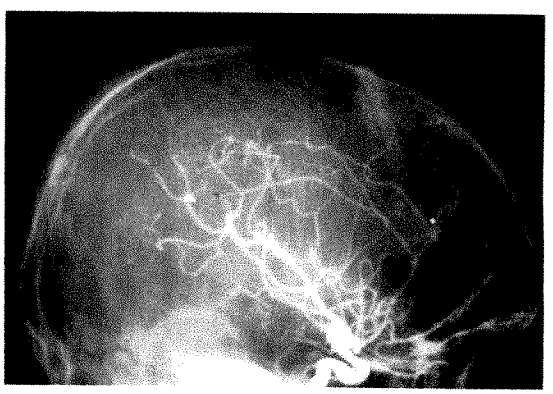


FIG. 9. Case II. Right lateral arterial phase. Note abnormal vascularity of frontal polar artery.

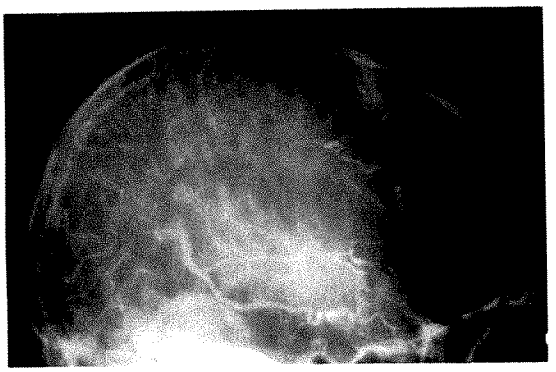


Fig. 10. Case II. Lateral late arterial phase with early venous drainage anteriorly and into basal vein and central venous system.

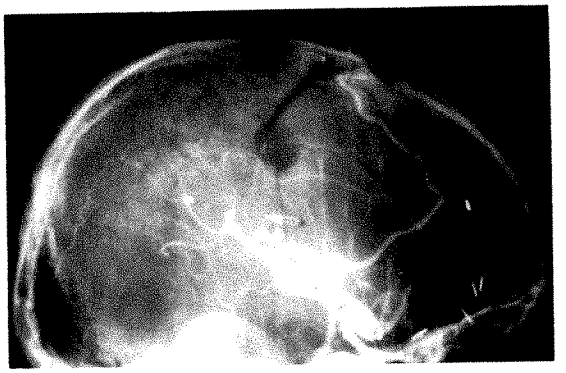


Fig. 12. Case II. Postoperative lateral arterial phase. Note absence of abnormal frontal polar artery.

corticosteroid preoperative preparation, a right frontal craniotomy was performed on April 6. An intracerebral hematoma was found, but because of the preoperative suspicion of an intrinsic malignancy, a prefrontal lobectomy was performed. Histologic examination revealed no evidence of neoplasia but rather the presence of a definite arteriovenous malformation. His postoperative course was totally benign and on return from convalescent leave he had repeat carotid angiography which failed to demonstrate any residual abnormal vascularity (Fig. 12). He was returned to duty.

DISCUSSION

Preoperatively both cases were considered to have the angiographic criteria of vascular malignant neoplasms. These included obvious major vessel displacements, vascular proliferation and contribution of these abnormal vessels to the tumor, and the presence of contrast medium in the late arterial and capillary phases within draining cerebral veins, indicating intrinsic arteriovenous shunting.

Study of these angiograms (Fig. 13 and 14) revealed an unusual "feathering" of the arterial branches of the major anterior cerebral arteries associated with the anomaly and the space-occupying mass. The mass in both cases was an intracerebral

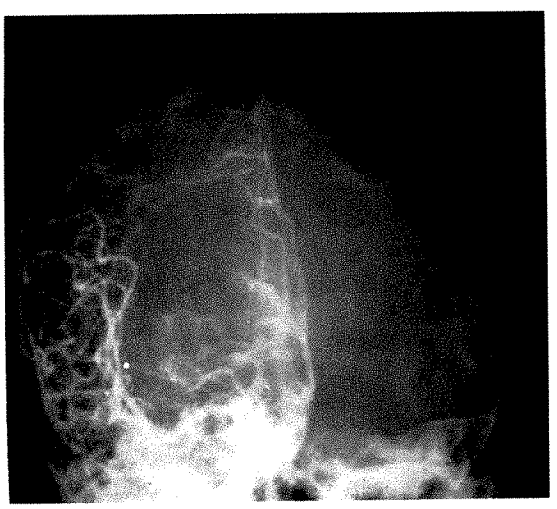


Fig. 11. Case II. Right half-axial, arterial phase with anterior cerebral artery displacement and abnormal vascularity.



Fig. 13. Close-up of "feathering" of callosal marginal artery—lateral view.

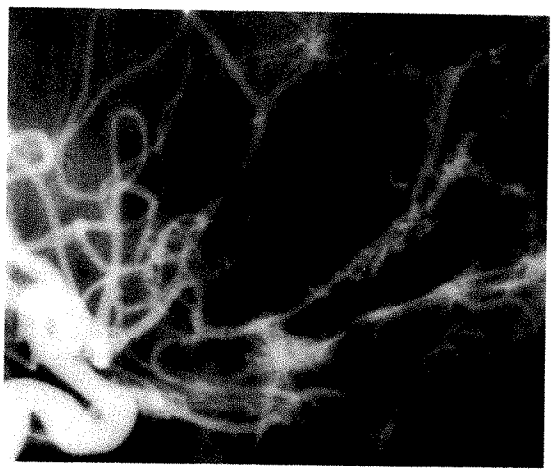


FIG. 14. Close-up of "feathering" of frontal polar artery—lateral view.

hematoma. The vascular "feathering" appearance was easily recognized on the surfaces of the frontal lobe of Case II at surgery.

As noted, the first case was operated upon, an intracerebral hematoma was found and removed and multiple areas of the hematoma wall were biopsied. Even when the permanent histologic sections revealed no evidence of neoplasia but the presence of an arteriovenous malformation, this pathologic diagnosis was questioned. The boy has been frequently evaluated during the past 2 years and he continues to be well without clinical evidence of a recurrent space-occupying mass.

The second case had an excisional prefrontal lobectomy and the entire specimen was subjected to histologic examination; neoplasia was not found. Both cases have been reviewed by the Armed Forces Institute of Pathology and classified as arteriovenous malformations.

These 2 cases are reported to alert other neurosurgeons and radiologists to the possibility that another angiographic appearance of a cerebral arteriovenous malformation may occur. This then, if recognized, or at least considered, could lead to a more appropriate surgical excisional procedure than the incorrect diagnosis of a cerebral malignancy, which could result in possible exclusion of or hesitation to perform corrective surgery.

SUMMARY

Two cases of histologically proven, angiographically similar cerebral arteriovenous malformations are reported which are apparently angiographically unlike other cerebral arteriovenous malformations and have criteria to suggest malignancy, which fortunately were false. The important feature appears to be a "feathering" of the abnormal arteries in conjunction with early regional venous drainage.

Neurosurgery Service
Walter Reed General Hospital
Washington, D. C. 20012

REFERENCES

1. CRAWFORD, J. V., and RUSSELL, D. S. Cryptic arteriovenous and venous hamartomas of brain. *J. Neurol., Neurosurg. & Psychiat.*, 1956, *19*, 1–11.
2. FRENCH, L. A., CHOU, S. N., and STORY, J. L. Cerebrovascular malformations. *Clin. Neurosurg.*, 1964, *11*, 171–182.
3. GILLINGHAM, J. Arteriovenous malformations of head. *Edinburgh M. J.*, 1953, *60*, 305–315.
4. KRAYENBÜHL, H., and SIEBENMANN, R. Small vascular malformations as cause of primary intracerebral hemorrhage. *J. Neurosurg.*, 1965, *22*, 7–20.
5. KRAYENBÜHL, H., and YAŞARGIL, M. G. Die Zerebrale Angiographie. Georg Thieme Verlag, Stuttgart, 1965.
6. OLIVECRONA, H., and LADENHEIM, J. Congenital Arteriovenous Aneurysms of the Carotid and Vertebral Systems. Springer-Verlag, Berlin, 1957.
7. OLIVECRONA, H., and RIIVES, J. Arteriovenous aneurysms of brain: their diagnosis and treatment. *Arch. Neurol. & Psychiat.*, 1948, *59*, 567–602.
8. PERRET, G., and NISHIOKA, H. Report on cooperative study of intracranial aneurysms and subarachnoid hemorrhage. Section VI. Arteriovenous malformations. *J. Neurosurg.*, 1966, *25*, 467–490.
9. POTTER, J. M. Angiomatous malformations of brain: their nature and prognosis. Hunterian Lecture. *Ann. Roy. Coll. Surgeons, England*, 1955, *16*, 227–243.
10. TAVERAS, J. M., and WOOD, E. H. Diagnostic Neuroradiology. Williams & Wilkins Company, Baltimore, 1964.

ANEURYSMS OF THE SUPERFICIAL TEMPORAL ARTERY*

By CHARLES B. WILSON, M.D.†
LEXINGTON, KENTUCKY

OF 10 superficial temporal artery aneurysms reported in the literature in the last 35 years, only 1 was diagnosed by carotid angiography.[4]

The angiographic features of this aneurysm deserve description for 2 reasons: (1) angiography provides an excellent means for establishing the diagnosis; and (2) someone unfamiliar with the aneurysm might be misled by its angiographic appearance.

REPORT OF A CASE

A 19 year old male student was referred to the University of Kentucky Hospital because of headache and a lump over the left temple. In a fight 6 weeks earlier he had been severely beaten about the head. He had not lost consciousness, and for 2 weeks thereafter suffered no sequelae. He then developed headaches of gradually increasing severity. As swelling receded from the left side of his face and scalp, he noticed a painless, nontender lump in the left preauricular area. The lump had enlarged since its discovery. He denied other complaints.

Physical examination revealed a pulsatile mass, 1.5 cm. in diameter, overlying the left temple (Fig. 1). Compression of the superficial temporal artery below the mass stopped its pulsations. No other abnormality was detected.

Left carotid angiography was undertaken with a provisional diagnosis of superficial temporal artery aneurysm and suspicion of a subdural hematoma. The angiograms demonstrated an aneurysm arising from the superficial temporal artery (Fig. 2, *A*, *B* and *C*).

The aneurysm was excised the next day. One afferent and 2 efferent arteries were identified and divided. Following excision, the aneurysmal sac measured 1.5×1×0.6 cm. (Fig. 3). The tough wall of this aneurysm was 3 mm. in thickness, and on microscopic examination consisted of granulation tissue and a dense fibrous coat. The wall of the parent artery terminated abruptly at the edge of the aneurysm and did not enter into its formation.

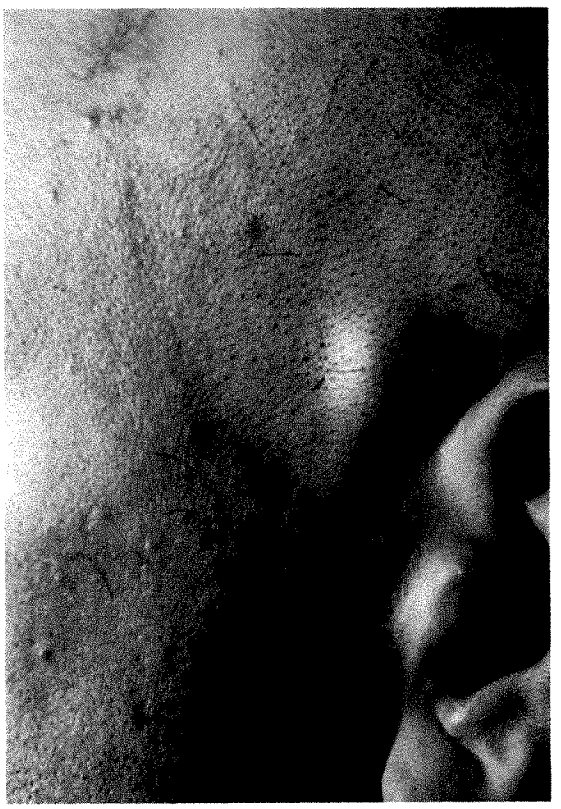


FIG. 1. Photograph of the patient showing aneurysm beneath the preauricular scalp.

The patient's headaches disappeared promptly and he returned to school.

DISCUSSION

Winslow and Edwards[3] reviewed the cases recorded through 1934, and more recent reports[3,4] give a contemporary view of this superficially situated aneurysm. Therapeutic temporal arteriotomy and dueling with swords once provided a significant number of cases, and their disappearance explains the rarity of temporal artery aneurysms in the recent past.

* From the Department of Surgery, Division of Neurosurgery, University of Kentucky, School of Medicine, Lexington, Kentucky.
† Present Address: Division of Neurological Surgery, University of California Medical Center, San Francisco, California.

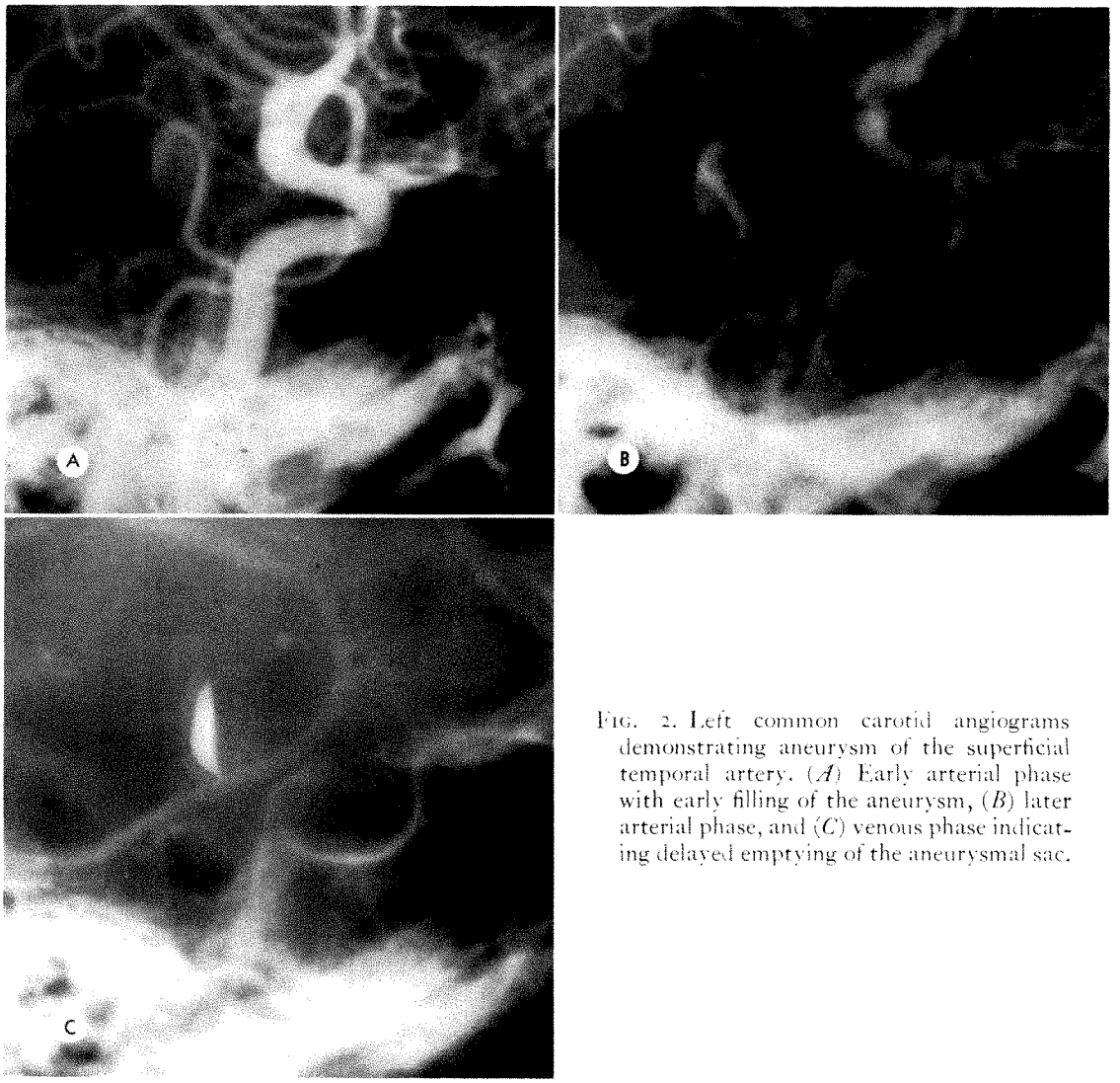


FIG. 2. Left common carotid angiograms demonstrating aneurysm of the superficial temporal artery. (*A*) Early arterial phase with early filling of the aneurysm, (*B*) later arterial phase, and (*C*) venous phase indicating delayed emptying of the aneurysmal sac.

Blunt trauma injures the superficial temporal artery as the vessel courses across the sharp edge of the superior temporal line, although in the present case the aneurysm involved the artery at a less vulnerable point within the temporal fossa. A through-and-through tear of the vessel wall allows extravasation of blood, the rapid appearance of a pulsating hematoma, and, with organization of the clot, a false aneurysmal sac. Although a review of reported cases indicates that the foregoing series of events describes the usual pathogenesis of these aneurysms, an incomplete tear of the artery may weaken the wall and in the course of time lead to aneurysmal dilatation at the point of injury.[3]

In the usual case physical examination reveals a pulsatile round mass, 1–2 cm. in diameter, above the lateral third of the eyebrow. Pulsation of the mass stops during compression of the superficial temporal artery at the zygomatic arch. Should thrombus fill much of the sac, pulsation may be faint or absent,[2] and the nature of the mass may be unsuspected. A cystic or solid mass, such as a sebaceous cyst, may transmit the pulsations of an underlying artery, and in at least one case an aneurysm of the middle meningeal artery eroded to

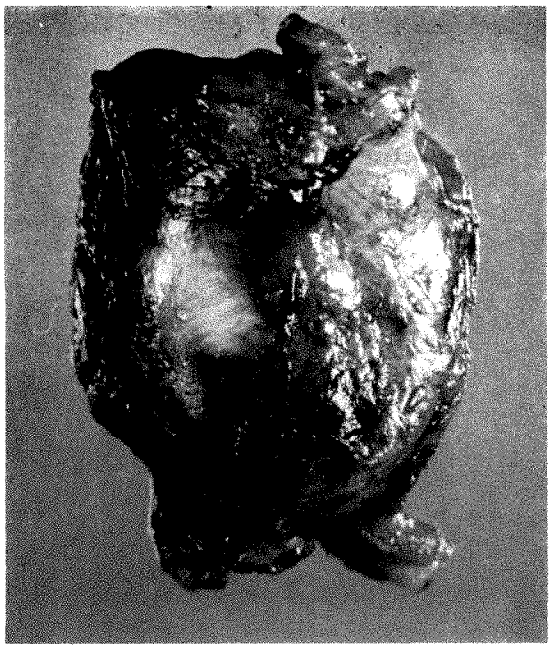


FIG. 3. Excised aneurysm. Large afferent artery is seen at the lower right edge of the sac, and the 2 efferent arteries are seen along the upper edge.

appear as a pulsating mass at the same site.

If the history of injury and the physical findings are typical, angiography hardly seems necessary unless indicated on other grounds, as in the present case. Common or external carotid angiography does provide certain identification of the aneurysm. Recognition of this lesion, specifically its differentiation from a traumatic aneurysm of the middle meningeal artery, assumes importance in the event of carotid angiography undertaken because of acute head injury.

Wortzman[6] reported the only previously described case documented by carotid angiography. As in the present case suspicion of an intracranial hematoma constituted the indication for angiography. Angiograms in both cases delineated the aneurysm and illustrated delayed emptying of the opacified sac for several seconds after transit of the contrast substance through the parent vessel. Others[4] have suggested that failure to opacify the aneurysm by carotid angiography justifies direct percutaneous injection of a suspected aneurysm, but this method carries unnecessary risk.

The patient with an aneurysm of the superficial temporal artery requires treatment for one of two reasons: either throbbing discomfort is annoying or the mass is unsightly. Since no authentic example of spontaneous cure is known, excision of the aneurysm, easily accomplished under local anesthesia, is indicated.

SUMMARY

Post-traumatic aneurysms of the superficial temporal artery are encountered infrequently, and the literature contains only one example diagnosed by carotid angiography.

An additional case is reported in which the aneurysm was demonstrated angiographically and treated by excision.

The clinical features of this condition are briefly discussed.

Division of Neurological Surgery
University of California Medical Center
San Francisco, California 94122

REFERENCES

1. BERK, M. E. Aneurysm of middle meningeal artery. *Brit. J. Radiol.*, 1961, *34*, 667–668.
2. DAVIES, D. G. L. Traumatic aneurysm of superficial temporal artery. *Brit. J. Surg.*, 1962, *49*, 343–344.
3. GITTES, R. F., and KARTCHNER, M. M. Posttraumatic temporal artery aneurysm: recurrent surgical curiosity. *A.M.A. Arch. Surg.*, 1963, *87*, 398–400.
4. HITE, S. J., GROVES, R. A., and SHARKEY, P. C. Superficial temporal artery aneurysms. *Neurology*, 1966, *16*, 1044–1046.
5. WINSLOW, N., and EDWARDS, M. Temporal aneurysm: analysis of cases reported in literature to June 1, 1934, and report of case of traumatic origin. *Am. J. Surg.*, 1935, *28*, 696–702.
6. WORTZMAN, G. Traumatic pseudo-aneurysm of superficial temporal artery: case report. *Radiology*, 1963, *80*, 444–446.

POSTERIOR FOSSA ANEURYSMS PRESENTING AS MASS LESIONS*

By H. F. W. PRIBRAM, M.D., D.M.R.D.,† J. D. HUDSON, M.D.,‡
and ROBERT J. JOYNT, M.D.§
IOWA CITY, IOWA

IN THE differential diagnosis of posterior fossa tumors, the distinction of extrinsic from intrinsic tumors is of paramount importance. Posterior fossa aneurysms may attain considerable size and present as expanding masses without history of bleeding. They may simulate extrinsic, intrinsic or intraventricular tumors. The roentgenologic diagnosis of such aneurysms may present equal difficulty with the clinical diagnosis. A mistaken diagnosis of pontine tumor may result in inappropriate radiation therapy, while an erroneous diagnosis of angle tumor may prove disastrous.

Vertebral angiography is seldom the procedure of choice in the investigation of posterior fossa tumors and is restricted to the diagnosis of meningiomas, hemangioblastomas, aneurysms and arteriovenous malformations. Nevertheless, we wish to emphasize its importance in the investigation of any posterior fossa mass which could conceivably be an aneurysm or malformation of the vertebro-basilar circulation. In this respect, the importance of vertebral angiography rivals that of carotid angiography in the exclusion of cavernous aneurysm simulating craniopharyngioma or pituitary tumor.

REPORT OF CASES

CASE 1. L.R., a 71 year old male with a firm clinical diagnosis of left cerebellopontine angle tumor had complained of deafness in the left ear and difficulty in balance for 3–4 years. In 1959 an idiopathic left lateral rectus palsy was corrected surgically. An audiogram showed high frequency tone loss on the left and there was no caloric response. Air and bone conduction tests indicated left-sided nerve deafness. Intermittent rotatory and vertical nystagmus as well as some coarse horizontal nystagmus was noted on left lateral gaze. There was flattening of the left nasolabial fold, and distinct weakness of the masseter muscle. Corneal sensation was decreased on the left, and there was some diminution to pin-prick over the first and second divisions of the fifth nerve on the left.

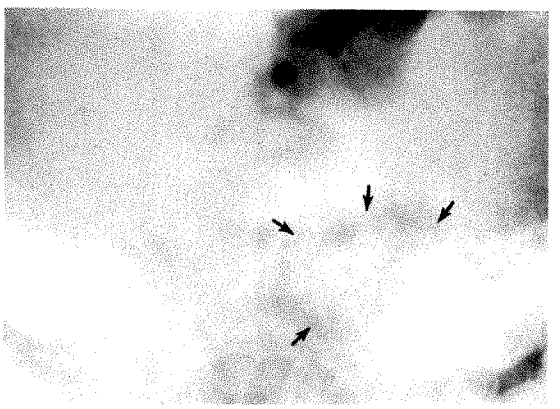


FIG. 1. Case 1. Air encephalogram showing a mass in the left cerebellopontine angle (arrows).

Air encephalography demonstrated flattening of the fourth ventricle which was displaced posteriorly. A mass was outlined in the left cerebellopontine angle (Fig. 1). Vertebral arteriography showed the angle mass to be a fusiform aneurysm (Fig. 2).

Unfortunately, after the second injection of contrast medium, the patient became unresponsive and developed laryngospasm. An emergency tracheotomy was performed and the patient began to improve. There was a residual right hemiparesis and complete expressive aphasia. Later he could blink his eyes and grip with the left hand on command, but he was never able to speak or move his right

* Presented at the Fifth Annual Meeting of the American Society of Neuroradiology, New York, New York, April 15, 1967.
From the Departments of Radiology (Neuroradiology) and Neurology, College of Medicine, University of Iowa, Iowa City, Iowa.
† Present Address: Professor of Radiology, Department of Radiology, Medical College of Virginia, Richmond, Virginia.
‡ Present Address: Austin Diagnostic Clinic, 801 W. 34th Street, Austin, Texas 78705.
§ Present Address: The University of Rochester Medical Center, 260 Crittenden Boulevard, Rochester, New York 14620.

side. He remained in this condition for about 3 days and then died.

At autopsy the aneurysm was again demonstrated and there were medullary and pontine hemorrhages. The patient also had an abdominal aortic aneurysm.

Comment. It is difficult to fault the clinical diagnosis, and the aneurysm was entirely unsuspected. This falls in the group of ectasias first described by Morgagni in 1769.

Case II. S.H., a 33 year old female, was admitted with intermittent diplopia and occipital headache. There was ptosis of the left upper lid and dilatation of the left pupil.

Left carotid arteriography showed elevation and medial displacement of the anterior choroidal artery. An air encephalogram showed slight posterior displacement of the aqueduct and fourth ventricle. A mass was outlined in the pontine cistern and the third nerve was shown to be stretched over the front of the mass. Vertebral arteriography showed the mass to be an aneurysm of the basilar artery.

The aneurysm was considered inoperable and the partial third nerve palsy and the diplopia improved. She had occasional headaches and intermittent tingling of the hands.



Fig. 2. Case I. Vertebral arteriogram showing the mass outlined at encephalography to be a fusiform aneurysm.



Fig. 3. Case III. Air encephalogram showing the deformity of the third ventricle and stretching of the aqueduct as found in intrinsic tumors of the pons.

Comment. This is an example of a true aneurysm of the basilar artery as first described by Cruveilhier in 1829. It is difficult to prognosticate, but these large aneurysms seldom bleed. On the other hand, there is always risk of brain stem infarction.

Case III. J.N., a 16 year old male, was admitted with personality changes and headache. A good student and athlete, he had begun to deteriorate markedly about a year prior to admission. He had progressive changes in his personality and loss of impulse control. There were several difficulties with the law, including stealing, accosting strange women in the street and fighting smaller children. His parents had noted that his gait had changed, becoming unsteady and spastic.

Air encephalography demonstrated symmetric flattening of the third ventricle and posterior displacement of the aqueduct. The appearances were those of an intrinsic tumor of the pons and midbrain (Fig. 3). Vertebral arteriography revealed a large basilar artery aneurysm (Fig. 4).

A ventriculo-caval shunt was performed to relieve the hydrocephalus. The patient tolerated the procedure well and showed some



FIG. 4. Case III. Vertebral arteriogram showing basilar artery aneurysm.

improvement; however, about a week following the operation he developed periods of unconsciousness and apnea and died shortly after.

Autopsy revealed hemorrhage from the previously demonstrated basilar artery aneurysm.

Comment. This is the youngest patient with a basilar artery aneurysm that we have seen, and it is interesting to note that these aneurysms are no respectors of age.

CASE IV. E.C., a 34 year old male, was admitted with complaints of headache and numbness of the face and right arm. His memory had deteriorated, he was becoming more irritable and he had progressive right-sided weakness. Physical examination showed some sensory loss of the entire right upper limb and right side of the face. Rapid alternating movements were performed poorly on the right.

Left carotid arteriography was normal. Air encephalography showed a smooth mass causing a defect in the posterior and inferior aspect of the third ventricle. Air partially outlined the mass.

The patient was found dead in bed the next morning and an autopsy showed the mass to be a posterior cerebral artery aneurysm.

Comment. The deterioration following lumbar puncture and encephalography has been commented upon by other authors. It is most likely due to midbrain infarction.

CASE V. E.M., a male, 49 years of age, was admitted with a history of right-sided occipital headache and hypertension of 8 years' duration, followed by transient right-sided hemiparesis and seizure.

Lumbar puncture showed no cells and a protein of 75 mg. per cent. Three hours following the lumbar puncture, he had acute onset of dyspnea, dysphagia, nystagmus, quadriplegia and expressive dysphasia. Tracheotomy was performed. He gradually improved and was discharged 6 weeks later with a diagnosis of basilar artery thrombosis, and was started on anticoagulants.

A year later he had an onset of diplopia and headache and was readmitted. Lumbar puncture showed a cerebrospinal fluid protein of 103 mg. per cent. An arteriogram demonstrated diffuse ectasia of the basilar artery (Fig. 5).

About 3 months following the arteriography, the patient became drowsy and dysarthric and complained of severe occipital headache. He was readmitted to the hospital and became unable to handle his secretions. Tracheotomy was performed. The patient died about a month after admission following several bouts of pneumonia.

Autopsy showed a large fusiform basilar artery aneurysm which filled the right cerebellopontine angle and compressed the brain



FIG. 5. Case V. Arteriogram showing fusiform basilar artery aneurysm.

stem. The aneurysm contained some old thrombus and there was widespread brain stem infarction.

Comment. This is another example of deterioration of a basilar artery aneurysm following lumbar puncture.

DISCUSSION

The incidence of intracranial aneurysms has been estimated as from 0.26 per cent to 4.9 per cent,[11] but has been reported as high as 10 per cent.[20] Many of these aneurysms rupture, although a large number remain silent clinically or produce symptoms other than subarachnoid hemorrhage. Some of these aneurysms are located in the posterior fossa and the incidence has been estimated to range from 7 per cent[21] to 23 per cent[26] with an average of 8 per cent.[7]

The symptomatology of posterior fossa aneurysms varies and depends on which structures are compressed and which vessel is involved; *e.g.*, the cerebellum, its efferent and afferent pathways may be affected, or the brain stem including the third to the twelfth cranial nerves. The motor tracts are more vulnerable to compression by an extrinsic mass such as an aneurysm than are the sensory pathways. This finding of pyramidal involvement with few sensory signs is considered by Alajouanine *et al.*[1] to be sufficiently common to be of diagnostic importance. The ventricular system may be obstructed producing hydrocephalus.

From a clinical and roentgenologic point of view, posterior fossa aneurysms should be classified as follows: (1) aneurysms presenting as subarachnoid hemorrhage; and (2) aneurysms presenting as posterior fossa mass lesions without history of bleeding. In general these will simulate pontine tumors,[18,24,25] cerebellopontine angle tumors,[4,7,12–14,16,28] or Ménière's disease.[6]

These aneurysms are of two types: true aneurysms (Cruveilhier 1829); and diffuse ectasias (Morgagni 1769) involving the vertebral and/or basilar artery.

True aneurysms are important from a surgical point of view since some of them are amenable to surgery. These are: posterior cerebral artery aneurysms; basilar aneurysms; and aneurysms of the vertebro-basilar junction.

SIGNS AND SYMPTOMS

There are no "classical" signs of a posterior fossa aneurysm. This is borne out by a review of some of the diagnoses made preoperatively or before angiography. Most frequent was a diagnosis of cerebellopontine angle tumor,[7,12,14,28] especially acoustic neurinoma,[4,16] pontine glioma[18,24,25] and "posterior fossa mass."[12,17,29] The latter is sufficiently broad to include an aneurysm, but is commonly excluded in the differential diagnosis of posterior fossa masses. Dandy[6] writes of the Ménière-like syndrome produced by posterior fossa aneurysm. Personality changes are frequently seen and in 2 of our patients a clinical diagnosis of vertebro-basilar insufficiency and psychosis was made. Others have faced a similar problem in diagnosis.

Globus and Schwab[12] diagnosed a patient as having bulbar encephalitis and another as meningoradiculoencephalitis, whereas a patient of Höök *et al.*[14] was diagnosed simply as "bulbopontine disease."

Focal pain due to an aneurysm of the posterior fossa is uncommon. Poppen[23] reported a case of "glossopharyngeal neuralgia" which was caused by a vertebral artery aneurysm. Dandy[6] as well as Eisenbrey and Hegarty[10] reported trigeminal neuralgia in association with an aneurysm of the posterior fossa. Less commonly, an aneurysm may mimic a cord lesion[27] or, as in Case IV, produce symptoms suggestive of a supratentorial lesion.

The most consistent symptom in patients with a posterior fossa aneurysm is headache. It is usually suboccipital and, as described by Yaskin and Alpers,[30] typically influenced by positional changes of the head. Disturbance of equilibrium and nystagmus due to compression of the cerebellum or its pathways, palsies of the third

through twelfth cranial nerves, and pyramidal tract involvement with minimal sensory impairment are also cardinal features of large unruptured posterior fossa aneurysms.

Due to the usual slow enlargement of the aneurysm or ectasia, there is often a prolonged history of intermittent and paroxysmal symptoms and signs.[1,14,30] A history of having suffered a "stroke" several months or years before more florid symptoms begin has been noted by Duvoisin and Yahr[7] and was seen in 1 of our patients (Case v).

If there is ventricular obstruction, such as in Case III, symptoms and signs of increased intracranial pressure usually occur requiring at least a shunting procedure if the aneurysm cannot be treated surgically. The ultimate fate of these aneurysms or ectasias which are not treated surgically may be respiratory failure due to brain-stem involvement or eventual rupture with subarachnoid hemorrhage. The diffuse ectasia, however, rarely ruptures.[20]

DIAGNOSTIC TESTS

The electroencephalographic findings are variable and consequently of little diagnostic importance. Occasionally, bifrontal activity is present as is often the case with posterior fossa lesions compressing the brain stem.[22]

The spinal fluid pressure is usually normal but may be elevated. The spinal fluid protein is often increased, as in Case I, strengthening the incorrect diagnosis of tumor. The color is usually clear unless the protein content is sufficiently high to induce xanthochromia.

Lumbar puncture, air encephalography and angiography may be hazardous in patients with large posterior fossa aneurysms.[8] Most, if not all, of our patients encountered some difficulty with one or the other of these procedures. Case I became hemiplegic during vertebral angiography. The third nerve paresis of Case II became worse following lumbar puncture. Case IV died following encephalography. Case V became quadriplegic following lumbar puncture.

ROENTGENOLOGIC FINDINGS

The greatest asset to the neuroradiologist is a suspicious mind. Any unusual posterior fossa mass, either from a clinical or roentgenologic point of view, should be considered an indication for vertebral angiography, as should sharply delineated or rounded masses, particularly when all or part is suspected of being extrinsic. Calcification is rare but when seen is obviously an indication for vertebral angiography.

Alleged intrinsic tumors referred to radiation therapy without surgical confirmation should have vertebral angiography performed regardless of age group. Some of these intrinsic tumors turn out to be aneurysms, while others are arteriovenous malformations. The findings of xanthochromic fluid and/or high cerebrospinal fluid protein in pontine tumors should arouse suspicion of aneurysm. Deterioration following lumbar puncture or air study should also suggest this possibility. Atypical cerebellopontine angle tumors require vertebral angiography.

Jannetta *et al.*[18] have previously drawn attention to suspicious findings at encephalography in cases of aneurysm of the vertebro-basilar circulation. These findings are: obliteration of the lateral recess of the fourth ventricle with only slight displacement and normal filling of the ventricular system without compression of the basal cisterns or tonsillar herniation.

SUMMARY

Aneurysms of the posterior fossa represent approximately 8 per cent of all intracranial aneurysms. These aneurysms may rupture to produce the familiar picture of subarachnoid hemorrhage, may be asymptomatic or may enlarge without rupturing to produce a multitude of neurologic symptoms. The diffuse ectasias of the vertebro-basilar system rarely rupture but may be indistinguishable clinically from a large aneurysm.

Posterior fossa aneurysms or ectasias may mimic cerebellopontine angle tumor, especially acoustic neuroma or pontine glioma and "posterior fossa mass." Less frequently, such an aneurysm or ectasia may precipitate a psychosis, trigeminal or glossopharyngeal neuralgia, or a spinal cord lesion.

The most characteristic clinical picture of a patient with a large unruptured posterior fossa aneurysm or ectasia is a prolonged, episodic and progressive course of cerebellar, pontine or medullary symptoms and signs. Headaches, disturbances of equilibrium, nystagmus, lower cranial nerve involvement and pyramidal signs with little sensory impairment should suggest the possibility of a posterior fossa aneurysm.

Vertebral arteriography should be performed in any patient in whom the clinical or roentgenologic findings suggest the possibility of a basilar artery aneurysm.

H. F. W. Pribram, M.D.
Department of Radiology
Medical College of Virginia
Richmond, Virginia 23219

REFERENCES

1. Alajouanine, T., LeBeau, J., and Houdart, R. La symptomatalogie tumorale des volumineux anéurysmes des artères vertébrales et basilaires. *Rev. neurol.*, 1948, *80*, 321–337.
2. Askenasy, H. M., Herzberger, E. E., and Wijsenbeek, H. S. Hydrocephalus with vascular malformations of brain: preliminary report. *Neurology*, 1953, *3*, 213–220.
3. Bladin, P. F., and Donnan, M. G. F. Cerebral arterial ectasia. *Clin. Radiol.*, 1963, *14*, 349–352.
4. Cape, C. Symptomatology of acoustic neurinomas. *GP.*, 1965, *32*, 116–121.
5. Cash, M. B., McGinnis, K. D., and Knighton, R. S. Posterior fossa arteriovenous aneurysm with calvarial change: case report. *Radiology*, 1966, *86*, 529–531.
6. Dandy, W. E. Pathologic changes in Ménière's disease. *J.A.M.A.*, 1937, *108*, 931–937.
7. Duvoisin, R. C., and Yahr, M. D. Posterior fossa aneurysms. *Neurology*, 1965, *15*, 231–241.
8. Dyke, C. G., and Davidoff, L. M. Significance of abnormally shaped subarachnoid cisterns as seen in encephalogram. Am. J. Roentgenol. & Rad. Therapy, 1934, *32*, 734–756.
9. Edwards, C. H., and Paterson, J. H. Review of symptoms and signs of acoustic neurofibromata. *Brain*, 1951, *74*. 144–190.
10. Eisenbrey, A. B., and Hegarty, W. M. Trigeminal neuralgia and arteriovenous aneurysm of cerebellopontine angle. *J. Neurosurg.*, 1956, *13*, 647–649.
11. Fields, W. S., and Sahs, A. L. Editors. Intracranial Aneurysms and Subarachnoid Haemorrhage. Charles C Thomas, Publisher, Springfield, Ill., 1965.
12. Globus, J. H., and Schwab, J. M. Intracranial aneurysms: their origin and clinical behavior in series of verified cases. *J. Mt. Sinai Hosp.*, 1942, *8*, 547–578.
13. Hoare, R. D. Arteriovenous aneurysm of posterior fossa. *Acta radiol.*, 1953, *40*, 96–102.
14. Höök, O., Norlén, G., and Guzman, J. Saccular aneurysms of vertebral-basilar arterial system: report of 28 cases. *Acta neurol. scandinav.*, 1963, *39*, 271–304.
15. Housepian, E., and Pool, J. L. Systematic analysis of intracranial aneurysms from autopsy file of Presbyterian Hospital, 1914–1956. *J. Neuropath. & Exper. Neurol.*, 1958, *17*, 409–423.
16. Hullay, J., and Tomits, G. H. Experience with total removal of tumors of acoustic nerve. *J. Neurosurg.*, 1965, *22*, 127–135.
17. Jamieson, K. G. Aneurysms of vertebrobasilar system: surgical intervention in 19 cases. *J. Neurosurg.*, 1964, *21*, 781–797.
18. Jannetta, P. J., Hanafee, W., Weidner, W., and Rosen, L. Pneumoencephalographic findings suggesting aneurysm of vertebral-basilar junction. *J. Neurosurg.*, 1966, *24*, 530–535.
19. Katf, N. Y., and Tatlow, W. F. T. Two cases of vertebral-basilar aneurysm. *Canad. M.A.J.*, 1965, *92*, 471–474.
20. McCormick, W. F. Personal communication.
21. McCormick, W. F., and Nofzinger, J. D. Saccular intracranial aneurysms: autopsy study. *J. Neurosurg.*, 1965, *22*, 155–159.
22. Paulson, G., Nashhold, B. S., Jr., and Margolis, G. Aneurysms of vertebral artery: report of five cases. *Neurology*, 1959, *9*, 590–598.
23. Poppen, J. J. Vascular surgery of posterior fossa. *Proc. Cong. Neurol. Surg.*, 1959, *6*, 198–209.
24. Spindle, D. K., and Abbott, K. H. Aneurysms arising from point of origin of vertebral artery. *Bull. Los Angeles Neurol. Soc.*, 1960, *25*, 130–139.
25. Steckel, R. J. Posterior fossa mass in 60-year-old woman. *J.A.M.A.*, 1965, *192*, 243–245.
26. Stehbens, W. E. Intracranial arterial aneurysms. *Australasian Ann. Med.*, 1954, *3*, 214–218.
27. Symonds, C. P., Meadows, S. P., and Taylor,

J. Compression of spinal cord in neighbourhood of foramen magnum, with note on surgical approach. *Brain*, 1937, *60*, 52–84.

28. WALTON, J. N. Subarachnoid haemorrhage. E. & S. Livingstone, Ltd., Edinburgh, 1956.
29. WEIBEL, J., FIELDS, W. S., and CAMPOS, R. J. Aneurysms of posterior cervicocranial circulation: clinical and angiographic considerations. *J. Neurosurg.*, 1967, *26*, 223–234.
30. YASKIN, H. E., and ALPERS, B. J. Aneurysm of vertebral artery: report of case in which aneurysm simulated a tumor of posterior fossa. *Arch. Neurol. & Psychiat.*, 1944, *51*, 271–281.

VOL. 105, NO. 2

VASCULAR MALFORMATIONS OF THE POSTERIOR FOSSA INCLUDING THE TENTORIAL HIATUS*

By LAWRENCE H. ZINGESSER, M.D., MANNIE M. SCHECHTER, M.D., E. LEON KIER, M.D., *and* MARK S. O'BRIEN, M.D.
BRONX, NEW YORK

VASCULAR malformations of the brain most often present clinically with subarachnoid hemorrhage and hemorrhage into the brain. This statement is also true for posterior fossa vascular malformations, but a significant number of posterior fossa malformations present another face to the clinician. For example, these lesions may present with the development of hydrocephalus or with progressive neurologic disability.[5] These lesions in infants may present clinically by causing congestive heart failure. Also these lesions may present with a bruit.

MATERIAL AND METHODS

The material forming the basis for this report consists of cases studied at the affiliated hospitals of the Albert Einstein College of Medicine over the last 6 years. There were 13 such cases during this interval. Five of these presented with subarachnoid hemorrhage, but another 5 presented with hydrocephalus and 1 presented with progressive neurologic disability (Fig. 1, *A–E*). Two infants presented with congestive heart failure. None of the cases presented with complaint of a bruit or pulsatile mass.

Most of the cases presenting with hydrocephalus and with progressive neurologic disability were studied primarily with air. This is the second roentgenologic examination, following the plain skull roentgenograms, with the air introduced either from below or from above. The etiologic diagnosis was not suspected in all of the cases following the air study. In one of the cases the correct diagnosis was unsuspected until the time of surgery, and postoperative angiography was carried out to demonstrate a partially resected malformation.

ROENTGEN FINDINGS

Hoare[3] has described certain changes which are evident on plain roentgenograms and should lead one to suspect an arteriovenous malformation of the posterior fossa. These are: (1) Increased vascular markings in the posterior part of the skull vault (Fig. 2); (2) enlargement of the foramina transversaria in the upper cervical vertebrae (Fig. 3); and (3) widening of the groove for the vertebral artery in the arch of the atlas, and enlargement of the jugular foramen (Fig. 4*A*).

Calcification might also be mentioned as a finding on plain roentgenograms, but this unfortunately is not present very often. In a paper reviewing features of the pathology of a large number of posterior fossa malformations, McCormick *et al.*[6] and others state that calcification was present in 12 of 164 of their cases, but was heavy in only 3 of the cases. This calcium deposit was within the walls of the vessels of the angiomas and was occasionally in the surrounding parenchyma. Bone formation was found in 2 cerebellar vascular malformations. The absolute specificity of these signs is open to question, and reliance on these findings individually is risky. For example, Pyo and Lowman[10] in their article on the arch of the first cervical vertebra underlying the transverse portion of the vertebral artery indicate that the sulcus may vary widely normally. In some of the patients the laminar margins showed little or no depression and in others the superior margin of the lamina was thick with a U-shaped sulcus present. The difficulties of

* Presented at the Sixty-ninth Annual Meeting of the American Roentgen Ray Society, New Orleans, Louisiana, October 1–4, 1968.
From the Department of Radiology, Albert Einstein College of Medicine, Bronx, New York.

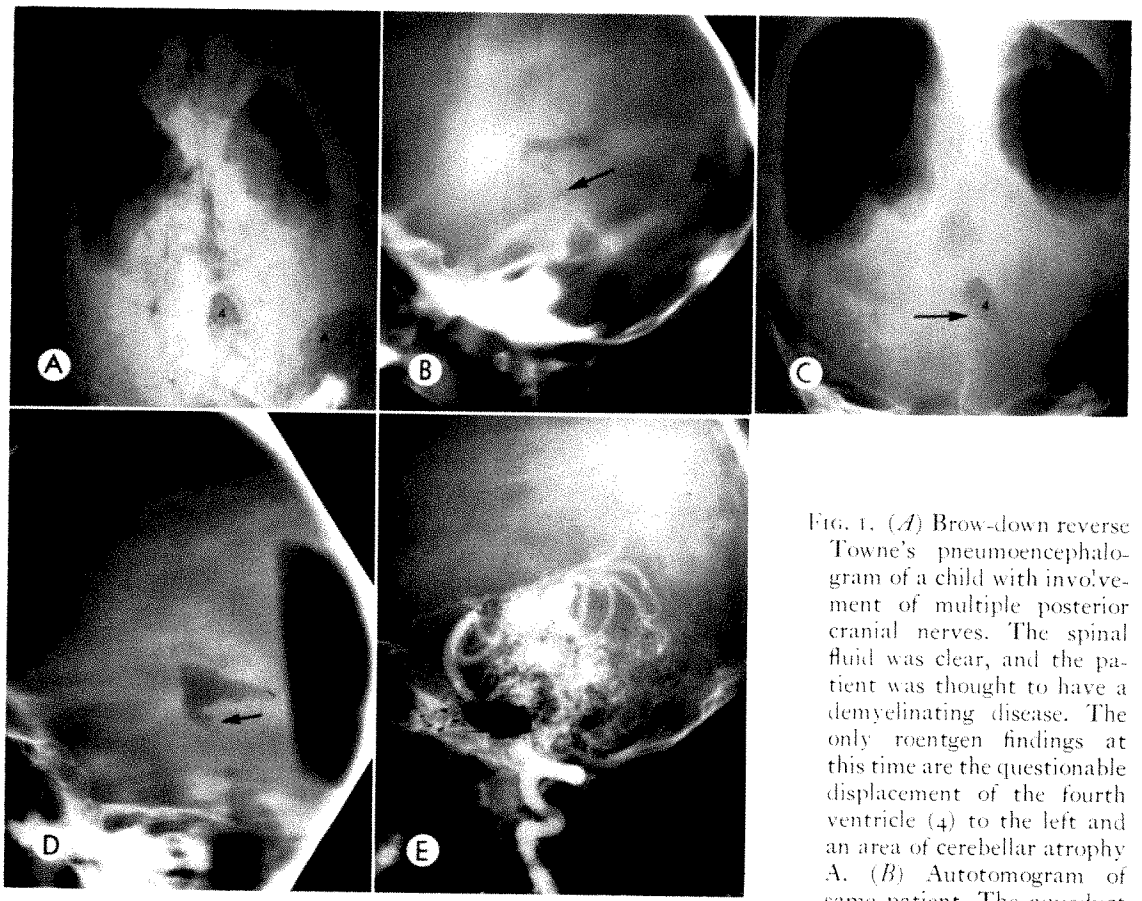


FIG. 1. (*A*) Brow-down reverse Towne's pneumoencephalogram of a child with involvement of multiple posterior cranial nerves. The spinal fluid was clear, and the patient was thought to have a demyelinating disease. The only roentgen findings at this time are the questionable displacement of the fourth ventricle (4) to the left and an area of cerebellar atrophy A. (*B*) Autotomogram of same patient. The aqueduct (black arrow) may be a little irregular at the point indicated by the arrow, but there is no definite displacement. (*C*) Brow-down reverse Towne's pneumoencephalogram of the same patient 4 years later. More cranial nerves were involved. At this time the fourth ventricle (4) is displaced to the left (black arrow). Note also the dilatation of the lateral ventricles. (*D*) Autotomogram showing partial aqueductal obstruction (black arrow) in this same patient. (*E*) Lateral vertebral angiogram of this patient following the air study in *C* and *D*. A large arteriovenous malformation fed by all cerebellar arteries is demonstrated.

interpretation of enlargement of the jugular foramen caused by variability are set forth well in an article by DiChiro *et al.*[3] The exocranial portion of the right jugular foramen ranges in size from 8-25 mm. by 5-15 mm., while the exocranial portion of the left jugular foramen ranges in size from 6-21 mm. by 4-16 mm. In DiChiro *et al.*'s cases of enlargement of the jugular foramen due to arteriovenous malformations, the pars vasculosa was increased in size with smooth well-outlined margins, while the pars nervosa was of normal shape and dimensions. The size of the foramen transversarium also is subject to great variability. According to Lindblom,[4] allowing for 15 per cent magnification, the average measurement is 8×10 mm. The evaluation of the skull for abnormal channels should include not only the area of the posterior fossa, but also the meningeal grooves supratentorially, as enlarged middle meningeal arteries may contribute to the supply of a malformation in the area of the tentorial notch. In the posterior fossa, attention should be paid not only to the presence of abnormal vascular grooves but also to enlargement of normal channels such as the channel for the lateral sinus on either side. There normally exists a great deal of

variation, but Lindblom[1] has established an upper limit for normal of 17 mm. here. (These grooves are visible according to Lindblom in 80 per cent of patients under 10 years.) Thus the neuroradiologist in evaluating skull roentgenograms of the patient in whom the vascular malformation of the posterior fossa is presenting with hydrocephalus or with progressive neurologic disability, usually will leave the examination of the skull roentgenograms with no clear idea about the presence of an arteriovenous malformation of the posterior fossa. Is the air study which follows going to indicate the correct diagnosis? There are certain features which may suggest the diagnosis.

In most of the cases in which hydrocephalus is seen in association with posterior fossa vascular malformations, the hydrocephalus is of the obstructive variety, but significant ventricular dilatation occurs in the absence of obstruction. The reason for the presence of nonobstructive hydrocephalus is unknown in a number of reported cases. In some cases of local dilatation of both the ventricular system and of the subarachnoid cisterns, the cause is atrophy.[7]



Fig. 2. Lateral roentgenogram of a patient presenting clinically with signs of a posterior fossa tumor. The spinal fluid was clear. The groove of the lateral and sigmoid sinuses is enlarged (20 mm.) (white arrows).

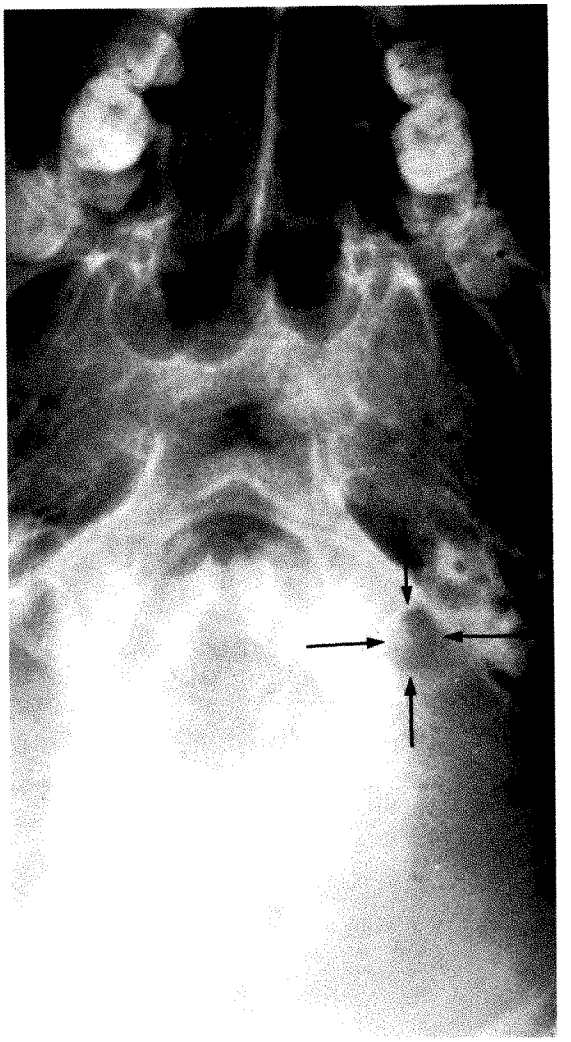


Fig. 3. Base view demonstrating enlargement of the left transverse foramen of the atlas (black arrows). The greatest diameter of this foramen is 13 mm. (upper limit of normal 8×10 mm.). This patient has a large arteriovenous malformation of the cerebellum.

Vascular malformations may cause obstruction of the ventricular system not only as a result of hemorrhage, in which case the presence of blood in the spinal fluid should lead to the performance of angiographic studies, but also as a result of the bulky vessels associated with the malformation.

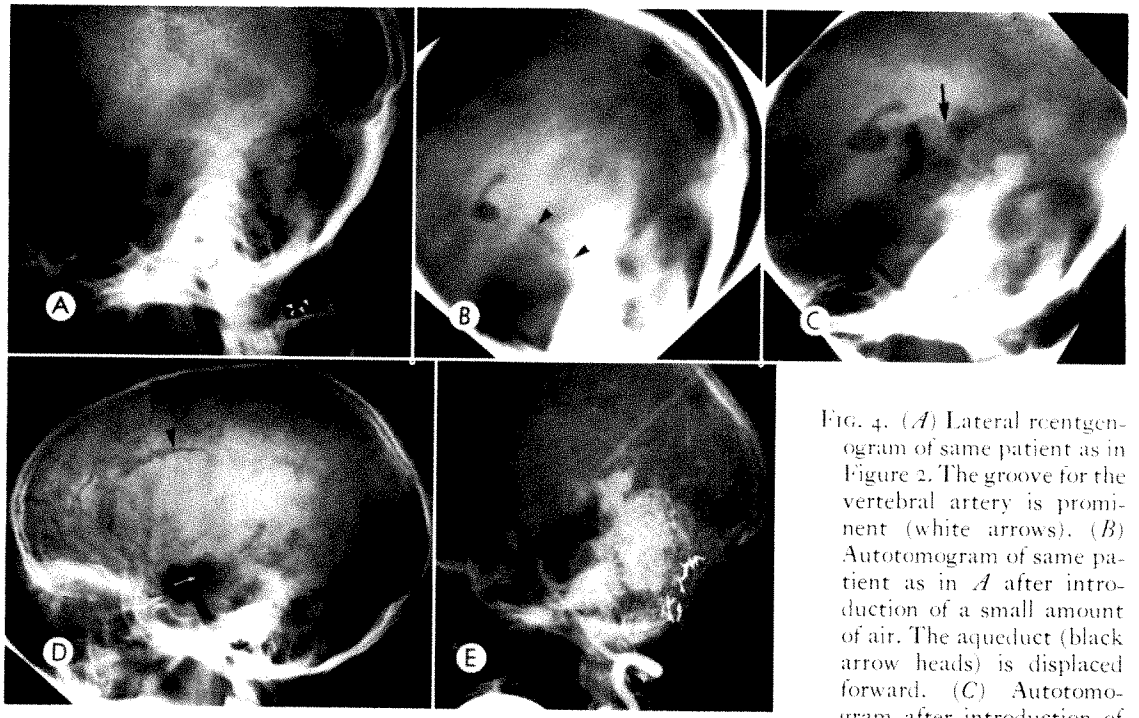


FIG. 4. (*A*) Lateral roentgenogram of same patient as in Figure 2. The groove for the vertebral artery is prominent (white arrows). (*B*) Autotomogram of same patient as in *A* after introduction of a small amount of air. The aqueduct (black arrow heads) is displaced forward. (*C*) Autotomogram after introduction of more air in same patient. The black arrow points to abnormal shadows in among the cerebellar folia. (*D*) Same patient. Very little air has entered the lateral ventricles, but air in a dilated pericallosal cistern (black arrowhead) indicates ventricular dilatation. Note that the terminal basilar artery (white arrow) is not enlarged. (*E*) Same patient. A large partially resected arteriovenous malformation is demonstrated postoperatively.

Enlarged feeding vessels may be outlined by air in the subarachnoid pathways (or by air in the ventricular system). Thus an enlarged basilar artery may cause an indentation in the floor of the third ventricle[11] or may be identified as enlarged as it courses through the pontine and interpeduncular cisterns. A mass of abnormal vessels may be identified in the cerebellopontine angle, or over the surface of the cerebellum (Fig. 4, *B–E*).

At times the saccular dilatation of draining veins may attain tremendous size. This is true especially in infancy and early childhood where the vein of Galen is involved in the vascular anomaly. Recently a report[2] on an aneurysm of the vein of Galen appeared in which the draining vessels and the vein of Galen itself had thrombosed. One of our cases had an aneurysm of the vein of Galen which demonstrated thrombosis of the draining channels but not of the aneurysmally dilated vein of Galen (Fig. 5, *A–G*). This patient presented with an enlarging head and with seizures. Extensive thrombosis is apparrently a rare feature of posterior fossa angiomas.[6] The diagnosis was suggested on the basis of pneumographic findings, and bilateral carotid angiography and vertebral angiography were carried out in order to demonstrate the supply to the malformation.

This is the second reported case of thrombosis of the draining vessels. This case is unique, however, in that the greatly dilated vein of Galen itself had not thrombosed. This particular lesion could only be confused with a giant aneurysm of the posterior cerebral artery.[9]

Angiography is required to establish the diagnosis in these cases. The malformations in the region of the tentorial notch frequently derive at least part of their supply from the carotid circulation. Branches from the internal carotid tree to the mal-

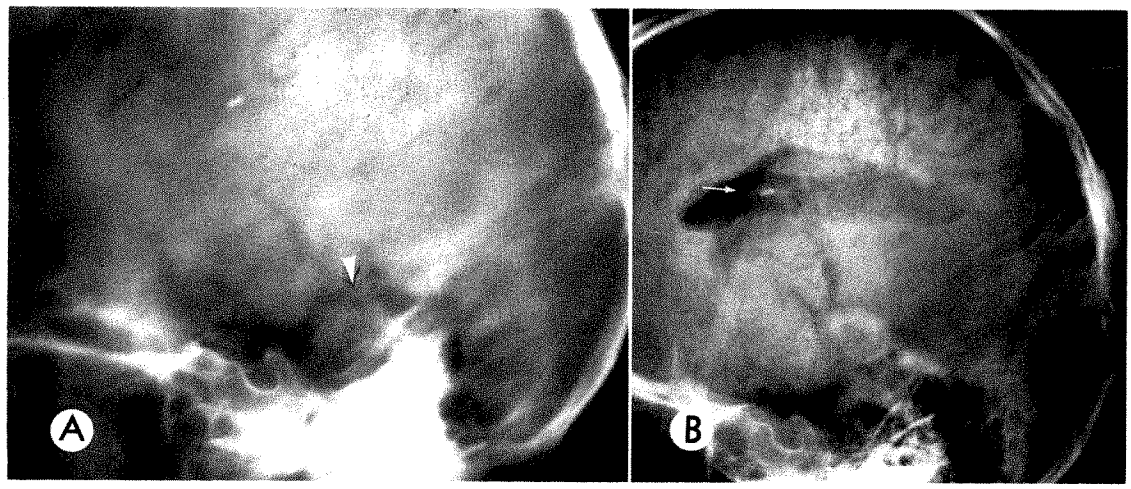
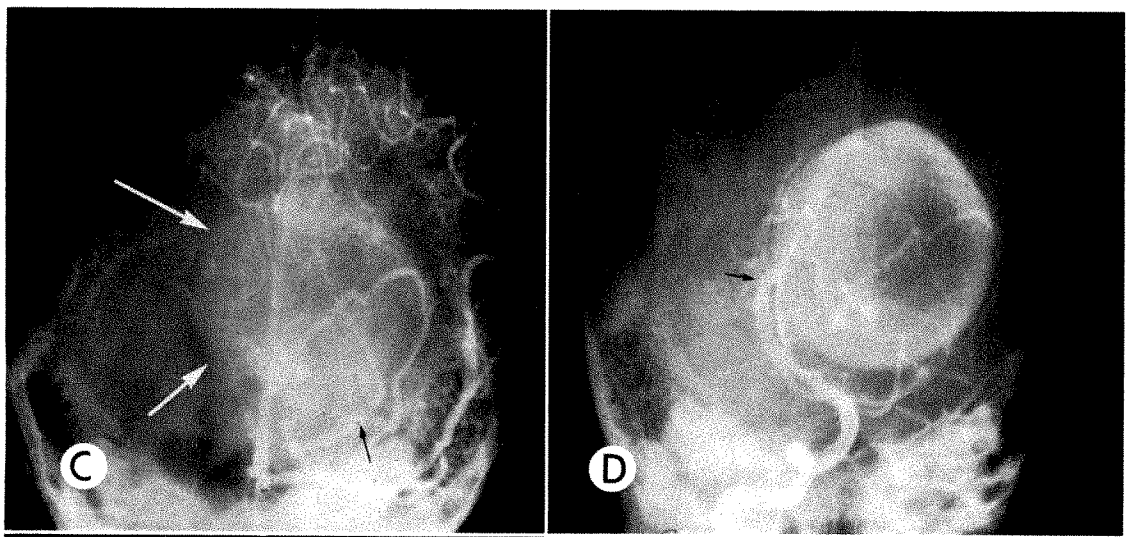


FIG. 5. (*A*) Autotomogram of a 5 year old who presented with a big head and with seizures. The spinal fluid was clear. There was no bruit. Air does not progress above the fourth ventricle. An abnormal cisternal shadow is indicated by the white arrowhead. (*B*) Same patient after introduction of air from above. This erect film demonstrates a large mass bulging into the ventricles (white arrow).



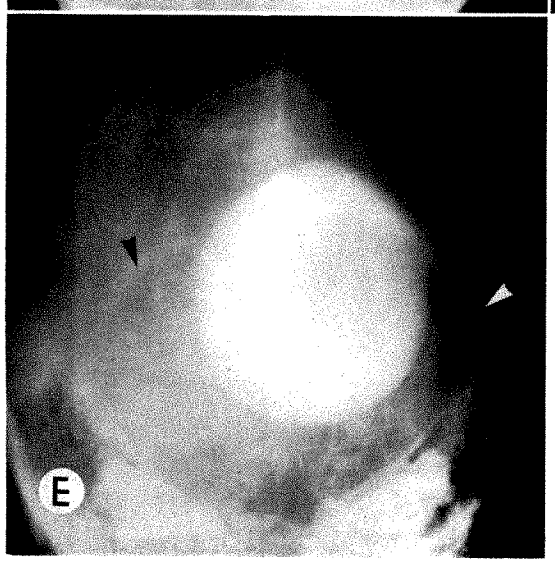


FIG. 5. (*C*) Left carotid angiogram, anteroposterior Towne's view, of the patient in *A* and *B*. A large vascular structure is filling with contrast (white arrows). The structure, which is an aneurysm of the vein of Galen, is filling here from the left posterior cerebral artery (black arrow). (*D*) Right vertebral angiogram, anteroposterior Towne view of same patient. Here the aneurysm of the vein of Galen is filling from the right posterior cerebral artery (black arrow). (*E*) Later phase of angiographic study in *D*. The aneurysm is now densely opacified. Note that the lateral sinuses (black and white arrowheads) are not enlarged.

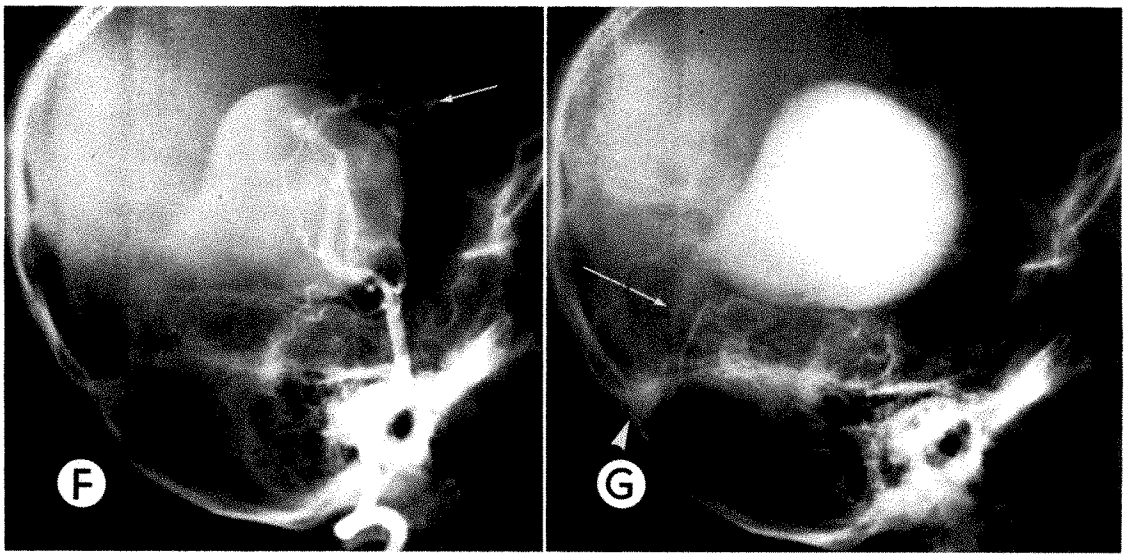


FIG. 5. (*F*) Lateral vertebral angiogram of same patient. Not only are the main stems of the posterior cerebral arteries filling the aneurysm of the vein of Galen, but enlarged choroidal arterial branches (white arrow) participate as well. (*G*) Later phase of angiographic series in *F*. The white arrow points to what is probably the remanent of the straight sinus. It does not drain into the torcular Herophili (white arrowhead), which is not enlarged.

formation include a tentorial branch from the cavernous portion of the internal carotid artery, branches of the anterior cerebral artery, and, if the posterior communicating artery is well developed, a supply from the posterior cerebral artery may be demonstrated to supply the malformation on carotid study. The middle meningeal artery may also be involved with the supply of an arteriovenous anomaly at the area of the tentorial notch. This may be suggested in plain roentgenograms by findings such as enlarged meningeal grooves with enlargement of the foramen spinosum.

A study of the posterior circulation will reveal feeders from one or more of the arteries to the cerebellum or brainstem or from dural vessels.[8]

CONCLUSIONS

Thirteen cases of vascular malformations involving the posterior fossa including the area of the tentorial notch have been reviewed.

The clinical presentation was either as subarachnoid hemorrhage, hydrocephalus, progressive neurologic disability or congestive heart failure.

When the clinical presentation was other than as subarachnoid hemorrhage or congestive heart failure, air studies were usually performed as the primary special procedure. In most cases plain skull roentgenograms did not indicate the etiology of the patients' condition.

Air studies may demonstrate a number of features which should indicate the need for angiography prior to surgical intervention. These are:

1. Demonstration of enlarged feeding vessels outlined by subarachnoid air and possibly by air in the third or fourth ventricle.
2. Demonstration of abnormal vessels outlined by subarachnoid air.
3. Localized atrophy.
4. Demonstration of a mass lesion in an area where an arteriovenous malformation may occur.

Lawrence H. Zingesser, M.D.
Department of Radiology
Albert Einstein College of Medicine
1300 Morris Park Avenue
Bronx, New York 10461

REFERENCES

1. DiChiro, G., Fisher, R. L., and Nelson, K. B. The jugular foramen. *J. Neurosurg.*, 1964, *21*, 447–460.
2. Heinz, E. R., Schwartz, J. F., and Sears, R. A. Thrombosis in the vein of Galen malformation. *Brit. J. Radiol.*, 1968, *41*, 424–428.
3. Hoare, R. D. Arteriovenous aneurysm of the posterior fossa. *Acta radiol.*, 1953, *40*, 96–102.
4. Lindblom, K. A roentgenographic study of the vascular channels of the skull with special reference to intracranial tumors and arteriovenous aneurysms. *Acta radiol.*, 1936, Suppl. 30.
5. Logue, V., and Monckton, G. Posterior fossa angiomas. *Brain*, 1954, *77*, 252–273.
6. McCormick, W. F., Hardman, J. M., and Boulter, T. R. Vascular malformations ("angiomas") of the brain with special reference to those occurring in the posterior fossa. *J. Neurosurg.*, 1968, *28*, 241–251.
7. McRae, D. L., and Valentino, V. Pneumographic findings in angiomata of the brain. *Acta radiol.*, 1958, *50*, 18–26.
8. Newton, T. H., Weidner, W., and Greitz, T. Dural arteriovenous malformation in the posterior fossa. *Radiology*, 1968, *90*, 27–35.
9. Obrador, S. O., Dierssen, G., and Hernandez, J. R. Giant aneurysm of the posterior cerebral artery. *J. Neurosurg.*, 1967, *26*, 413–416.
10. Pyo, J., and Lowman, R. The "ponticulus posticus" of the first cervical vertebra. *Radiology*, 1959, *72*, 850–854.
11. Sjogren, S. Percutaneous vertebral angiography. *Acta radiol.*, 1953, *40*, 113–127.

SELECTIVE THIRD VENTRICULAR CATHETERIZATION FOR PANTOPAQUE VENTRICULOGRAPHY*

By HAROLD A. WILKINSON, M.D.
BOSTON, MASSACHUSETTS

THE technique of selective catheterization of the third ventricle for air ventriculography was described in 1956 by Azambuja *et al.*[1] and has subsequently been modified to include the introduction of intraventricular pantopaque.[4] Although it enjoys some popularity in Europe and South America,[2,4,11] it has not been widely employed in this country.[3] The author was first introduced to third ventricular catheterization as an aid to pantopaque ventriculography by Dr. Alex MacIntyre, now of Liverpool, England. Although Taveras and Wood[10] mention third ventricular catheterization and discuss the use of positive contrast agents in ventriculography, they do not discuss the use of the two techniques in combination. The author has found selective third ventricular catheterization for pantopaque ventriculography to be rapid and safe and to offer certain distinct advantages, especially in patients suspected of harboring posterior fossa lesions.

The purpose of this report is to present a review of the technique and of the author's experience with it, and to focus additional interest on a potentially useful adjunct to the neuroradiologic diagnostic armamentarium.

METHOD

With the patient in the supine position, a frontal burr hole is drilled, generally over the nondominant hemisphere, centered 2.5 to 3.5 cm. lateral to the midline and just anterior to the coronal suture. After opening the dura and coagulating the pia in the usual fashion, a radiopaque No. 8 French hollow-tipped soft rubber catheter (or a No. 8 French Scott cannula of at least 10 cm. in length) is inserted with the aid of a stiff wire stylet into the frontal horn of the lateral ventricle. In the frontal projection, the catheter is directed toward the inner canthus of the ipsilateral eye. In the lateral projection, the catheter is directed toward a point on the zygoma midway between the lateral angle of the orbit and the external auditory canal. If previous arteriographic studies are available, a more accurate directing point may be provided by the junction of the thalamostriate vein with the internal cerebral vein.

Once the lateral ventricle has been entered, usually at a depth of 4 to 6 cm., the wire stylet is withdrawn and set aside. The catheter is then advanced without the stylet to its final depth of 8 to 10 cm. During this stage no additional resistance should be encountered; if increased resistance is encountered it is unwise to persevere for fear of initiating hemorrhage, perforating the lamina terminalis, penetrating the diencephalon, or occluding the aqueduct of Sylvius. Once the catheter is in place, its end is occluded with a sterile three-way stopcock.

Roentgenographic confirmation of third ventricular catheterization may be obtained either before or after suturing the burr hole. If a posterior fossa lesion is suspected, the salient portions of the ventriculogram are executed with the patient remaining in the supine position. Ten to 12 ml. of cerebrospinal fluid are then carefully withdrawn, the volume to be removed being in part dictated by the intracranial pressure. One-half to 2 ml. of pantopaque are then introduced and are followed by 10 to 20 ml. of oxygen or filtered room air. Without moving the patient, roentgenograms are then taken in the anteroposterior, Towne's and lateral projections (Fig. 1, *A* and *B*). If the

* From the Department of Surgery, Harvard Medical School, Boston, Massachusetts.

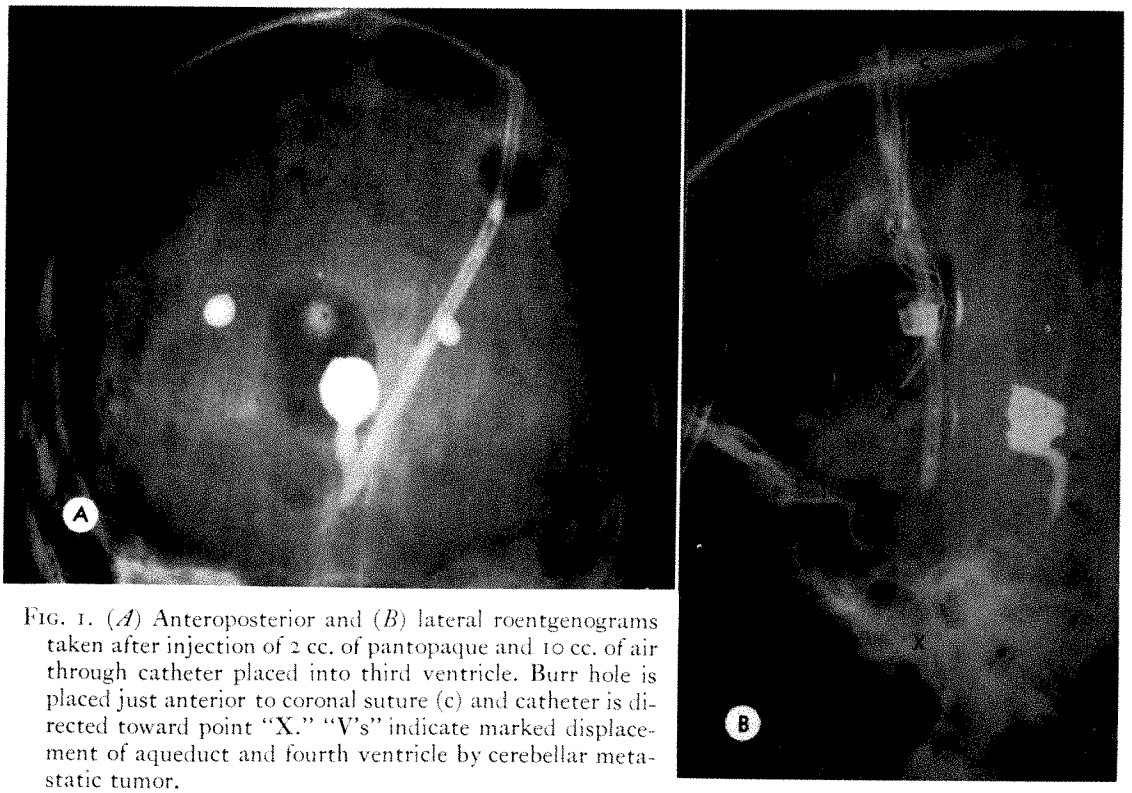


Fig. 1. (*A*) Anteroposterior and (*B*) lateral roentgenograms taken after injection of 2 cc. of pantopaque and 10 cc. of air through catheter placed into third ventricle. Burr hole is placed just anterior to coronal suture (c) and catheter is directed toward point "X." "V's" indicate marked displacement of aqueduct and fourth ventricle by cerebellar metastatic tumor.

pantopaque has not entered the fourth ventricle, either an additional increment of pantopaque may be added, or the head may be elevated slightly by flexion of the neck. It should always be kept in mind that subtotal aqueductal stenosis may block the passage of oily contrast materials temporarily, as Backmund and Decker have also observed.[2] Thus, when an apparent aqueductal obstruction is encountered—especially without aqueductal displacement—it is well to take delayed roentgenograms after gently manipulating the head.

Should the catheter *not* pass through the foramen of Monro into the third ventricle, of course the alternative always remains of doing a "standard" ventriculogram, including manipulating pantopaque from the frontal horn of the lateral ventricle into the third ventricle.

CLINICAL EXPERIENCES

In the past 3 years (1965–1968) the author has personally employed this technique in 12 patients and has supervised its use by members of the resident staff* in 5 others. These patients were derived from the Boston City Hospital, the Massachusetts General Hospital, the Boston Veterans Administration Hospital and the Winchester Hospital. Their diagnoses are listed in Table 1.

The ease of performance of this technique is evidenced by the success rate in the present series (88 per cent), which includes 4 successful studies performed by members of the resident staff who were previously unfamiliar with the technique. One failure of third ventricular catheterization occurred in a patient who had undergone previous frontal lobe surgery; the other occurred in a patient with a posterior third ventricular mass. Both studies were completed by manipulating pantopaque from the lateral ventricle through a distorted foramen of Monro into the third ventricle.

* Drs. Gerald Brodkey, Robert Cantu and Charles Brown.

TABLE I

LIST OF PATIENTS BY CONFIRMED DIAGNOSIS

No. of Patients	Diagnosis
4	Cerebellar metastatic tumor
3	Communicating hydrocephalus
2	Adult aqueductal stenosis
1	Adult Dandy-Walker syndrome
1	Cerebellar astrocytoma
1	Fourth ventricular glioblastoma
1	Craniopharyngioma
1	Suprasellar avascular meningioma
1	Avascular bifrontal glioma
1	Cerebellar arteriovenous malformation with hematoma
1	Posterior third ventricular tumor
17	Total

Two patients (12 per cent) suffered minor complications, although in neither case were there permanent sequelae. One patient, with metastatic carcinoma of the cerebellum, showed no apparent ill effects from unintentional perforation of the floor of the third ventricle. The study was completed successfully after the catheter had been withdrawn to its proper depth of 9 cm. The second patient, a 14 year old boy with a cystic cerebellar astrocytoma, did not fare so well. Shortly after having placed the ventricular catheter, and before roentgenograms could be taken, the neurosurgical team's attentions were usurped by an acute surgical emergency. Several hours later this patient rapidly lost consciousness and showed signs of cerebral pressure herniation. Roentgenograms which were then taken demonstrated the catheter to have passed through the third ventricle into the aqueduct of Sylvius—causing a mechanical aqueductal stenosis! Again the catheter was withdrawn to its proper depth (10 cm.) and both ventriculography and surgery proceeded uneventfully. Eighteen months later this boy was again playing basketball with his schoolmates. No patient has shown an untoward reaction to the intraventricular pantopaque, either immediate or delayed. The one patient who has to date come to postmortem examination showed no evidence of ventricular irritation or injury to the foramen of Monro.

DISCUSSION

The technique of third ventricular catheterization with pantopaque ventriculography has proved to be extremely useful, especially in patients suspected of harboring posterior fossa lesions. Positive contrast demonstration of the posterior third ventricle, aqueduct and fourth ventricle is obtained almost immediately following the first injection. Of course, the concomitant injection of oxygen or air should not be omitted. This allows both a demonstration of the severity of any hydrocephalus which might be present and a survey of the anterior third ventricle and both lateral ventricles for any possible associated abnormality.

Perhaps an even greater advantage of this technique is its ease and simplicity. The entire procedure from burr hole to roentgenography is done with the patient supine, preferably lying on the same table throughout. In the critically ill patient, or in the patient who is unconscious or unable to cooperate, this factor can be of paramount importance. Similarly, the advantages for the anesthetized patient seem apparent, although in the author's series all procedures were performed under local anesthesia. In patients who are alert and cooperative and for whose study a mechanically somersaulting pneumoencephalography chair is available, it is the author's practice to begin the study with air or oxygen alone, progressing to pantopaque only if further definition becomes necessary.

Positive contrast ventriculography with lipiodol or pantopaque has been in use since 1923[8,9] and several authors have commented on its safety—not uncommonly reporting less reaction and greater patient comfort following positive contrast ventriculography than following air ventriculography.[2,3,5,6,11] Strangely enough, me-

chanical emulsification of pantopaque seems greatly to increase its toxicity,[7,8] and probably should be avoided. In every case in this series the pantopaque was well tolerated. The 4 patients in whom ventriculoatrial shunts were subsequently placed experienced no unusual difficulties—an observation shared by Papatheodorou and Teng.[6]

In this series, at least, the procedure has proved to be quite safe. Hydrocephalus, which usually constitutes one of the indications for ventriculography, usually causes an enlargement of the foramen of Monro, thus facilitating both the ease and the safety of third ventricular catheterization. The two complications which did result were due to a failure to properly mark a 10 cm. point on the catheter prior to insertion. In both cases the catheter had been introduced too far, although in neither instance did permanent sequelae ensue. It is, however, extremely important that the stiff wire stylet be withdrawn prior to passing the catheter through the foramen of Monro. An increased resistance should not be ignored as a potential danger signal.

SUMMARY

The technique of selective third ventricular catheterization and pantopaque ventriculography is described and the author's experience with 17 cases is briefly summarized.

This technique has been found to be especially useful in patients suspected of harboring a posterior fossa lesion. Its chief advantages are the speed with which it can be executed and the avoidance of the necessity of manipulating the patient during the procedure (the entire procedure is done with the patient supine), the latter being of especial value in patients who are seriously ill, unable to cooperate or unconscious.

The procedure has proved to be safe, although several points of caution are discussed.

Neurosurgical Service
Sears Building-Third Floor
Boston City Hospital
818 Harrison Avenue
Boston, Massachusetts 02118

REFERENCES

1. Azambuja, N., Arana Iniguez, R., Sande, M. T., and Garcia Güelfi, A. Central ventriculography. *Acta Neurol. Lat. Am.*, 1956, *2*, 58–64.
2. Backmund, H., and Decker, K. Ventrikulographie mit positiven Kontrastmitteln. *Fortschr. a. d. Geb. d. Röntgenstrahlen u. d. Nuklearmedizin*, 1963, *99*, 173–179.
3. Glasauer, F. E. Pantopaque ventriculography: its diagnostic and prognostic value. *J. Canad. A. Radiologists*, 1965, *16*, 125–131.
4. Nadjmi, M., and Schaltenbrand, G. Gezielte Darstellung des Dritten Ventrikels mit Pantopaque. *Acta radiol.* (Diag.), 1963, *1*, 881–885.
5. Pansini, A., Djindjian, R., and Hurth, M. Primauté de l'iodo-ventriculographie dans le diagnostic topographique de certaines lésions expansives de la fosse postérieure. *Ann. radiol.*, 1963, *6*, 831–864.
6. Papatheodorou, C. A., and Teng, P. Air-pantopaque ventriculography in congenital hydrocephalus and myelomeningocele. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1964, *91*, 647–655.
7. Portera-Sanchez, A., Bravo, G., and Parera, C. Emulsified pantopaque ventriculography. *J. Neurosurg.*, 1964, *21*, 422–423.
8. Sicard, J. A., and Forestier, J. Roentgenologic exploration of central nervous system with iodized oil (lipiodol). *Arch. Neurol. & Psychiat.*, 1926, *16*, 420–434.
9. Sicard, J. A., Paraf, J., and Laplane, L. Radiodiagnostic rachidien lipiodolé: ponction atloido-occipitale et cervicale. *Presse méd.*, 1923, *31*, 885–887.
10. Taveras, J. M., and Wood, E. H. Diagnostic Neuroradiology. Williams & Wilkins Company, Baltimore, 1964.
11. Viñas, F. J. Iodoventriculography by direct catheterization of third ventricle in posterior fossa lesions of childhood. *J. Neurosurg.*, 1964, *21*, 492–496.

IDIOPATHIC FAMILIAL CEREBROVASCULAR FERROCALCINOSIS (FAHR'S DISEASE) AND REVIEW OF DIFFERENTIAL DIAGNOSIS OF INTRACRANIAL CALCIFICATION IN CHILDREN*

By DONALD P. BABBITT, M.D.,† T. TANG, M.D.,‡ J. DOBBS, M.D.,§ *and* R. BERK, M.D.‖
MILWAUKEE, WISCONSIN

THE roentgenographic finding of irregular punctate areas of intracranial calcification with associated clinical manifestations of severe growth disorder, progressive mental deterioration, and familial occurrence suggests a diagnosis of idiopathic familial cerebrovascular ferrocalcinosis (Fahr's disease).[5] This disease was identified and studied in 3 siblings, the only children of normal parents. Of these 3 patients, the 2 males showed the clinical characteristics of the disease and intracranial calcification on skull roentgenograms at the age of 5 months, while the female died suddenly of an overwhelming bilateral pneumonia at the age of 6 weeks without roentgenographic studies or overt clinical evidence of the disease. However, postmortem examination of the female infant revealed microscopic ferrocalcinosis in the arterioles and venules of the centrum, cerebellum and basal ganglia. The living male has been studied extensively for known causes of retardation and intracranial calcification with negative results. The other male expired at the age of 4 years and demonstrated microscopic ferrocalcinosis in the arterioles and venules of the brain similar to those found in the 6 week old female. In addition, the 4 year old child demonstrated positive P.A.S. staining in the same areas, indicating conjugation of the iron and calcium with glycoprotein. Karyograms on the 3 siblings and parents were normal.

REPORT OF CASES

CASE I. This 5 month old boy was admitted to the Milwaukee Children's Hospital on July 21, 1963 because of retardation. At birth he was thought to be normal, but was noted to be "jittery." His height and weight were at the third percentile. His head circumference was below the third percentile. He had evidence of brain damage, the manifestations of which were central blindness, a rigid form of cerebral palsy, and profound mental retardation. Examination of the fundi revealed areas of pigment loss with gray areas in the retina. Laboratory studies were done; the only abnormality noted was that the spinal fluid had 43 leukocytes and a total protein of 60 mg. per cent.

Roentgenography of the skull showed multiple scattered areas of calcification most dense in the basal ganglia. The electroencephalogram was reported as abnormal with diffuse slow activity. He was readmitted 2½ years later because of a convulsive episode consisting of twisting of the extremities and the head, and jerky eye movements, indicating further deterioration which has continued up to the present. This is the only child alive at the time of this report.

CASE II. The sister of Case I was born on February 19, 1964. She appeared to be normal at birth. She did well until a week before admission when chest congestion developed. On the day of admission she had increased difficulty breathing and anorexia. In the physician's office, cardiac arrest occurred. Resuscitation was accomplished, and the infant was sent to Milwaukee Children's Hospital where she was noted to be critically ill with

* From the Milwaukee Children's Hospital and Marquette University School of Medicine, Milwaukee, Wisconsin.
† Director, Department of Radiology, Milwaukee Children's Hospital; Associate Professor of Radiology, Marquette University School of Medicine.
‡ Assistant Professor of Pathology, Marquette University School of Medicine.
§ Assistant Professor of Pediatrics, Marquette University School of Medicine; Head of Special Development Clinic, Milwaukee Children's Hospital.
‖ Assistant Clinical Professor of Pediatrics, Marquette University School of Medicine.

irregular grunting respiration and an apical rate of 60 per minute. Chest roentgenography showed severe extensive bilateral bronchopneumonia. She died 6 hours after admission, at the age of 6 weeks. Postmortem examination revealed extensive bilateral bronchopneumonia and microscopic ferrocalcinosis in the arterioles and venules of the centrum, cerebellum and basal ganglia.

Case III. This child was admitted to Milwaukee Children's Hospital on October 17, 1965, at the age of 5 months, because of seizures. He appeared to be normal at birth and the parents thought that his development had been essentially normal until the age of 4 months, when he appeared to regress. He stopped smiling. He no longer rolled over. He had become quite "jittery" with shaking of his arms and legs. He developed a high pitched cry and irritability.

Physical examination revealed him to be in the fifteenth percentile for height and weight, and his head size was in the third percentile. His eyes did not react to light. He was unaware of his surroundings, had poor head control, and had increased tone in all extremities. Funduscopic examination was normal.

Examination of the cerebrospinal fluid showed the presence of 15 leukocytes and 55 mg. per cent protein. The electroencephalogram was noted to be abnormal with considerable slowing. Skull roentgenography showed multiple calcifications diffusely scattered throughout the brain substance. Pneumoencephalography was attempted but was not satisfactory.

The extensive laboratory studies were as follows: The calcium was 4.6 mg. per cent, the phosphorus 1.9 mg. per cent, the LDH 68 units per milliliter, and the colloidal gold curve 12222100000. The spinal fluid was negative for inclusion bodies, protozoa, bacteria or fungus organisms. Subdural taps yielded a small amount of blood on the left side which showed no growth on culture. The blood studies showed that the hemoglobin was 11.2 gm. per cent, white blood cell count 14,200, erythrocyte sedimentation rate 22 mm. per hour, fasting blood sugar 76 mg. per cent, and blood urea nitrogen 9 mg. per cent. The serum electrolytes showed a sodium of 134 mEq/L., potassium of 4.9 mEq/L., a CO_2 of 18.4 mEq/L., chlorides of 106 mEq/L., and a pH of 7.39. Serum calcium was 9.2, 9.6 and 9.4 mg. per cent, serum phosphorus 6.4, 5.7 and 5.6 mg. per cent, phosphatase levels 5.9, 8.0 and 10.6 King-Armstrong units, and protein-bound iodine 9.4 μg./100 ml. The urinalysis was negative and the Sulkowitch test was negative three times. A urine smear was negative for giant cells and inclusion bodies. The chromosome studies showed a normal male chromosomal pattern. Amino-acid chromatography on the urine was normal. The VDRL was nonreactive. Serum bilirubin level was 1.8 mg. per cent. The toxoplasmin skin test and Sabin dye test were negative.

This child died at the age of 4 years. The final pathologic summary stated that this 4 year old white boy had familial cerebrovascular ferrocalcinosis and died of recurrent aspiration pneumonia and acute hemorrhagic pancreatitis.

DISCUSSION

This particular form of intracerebral calcification, often referred to as idiopathic non-arteriosclerotic intracerebral calcification, or as "Fahr's disease," has been known to pathologists since 1855, when Bamberger[1] described extensive calcification in both hemispheres in a 34 year old woman. In 1875 Elischer[4] described calcification in the basal ganglia in a patient, and other similar cases were reported by Mallory[10] in 1896, von Hanseman[14] in 1899, and Geyelin and Penfield,[8] who in 1929 studied a family of 4 siblings with intracerebral calcification. Fahr[5] in 1930 reported the case of a 50 year old man under the title of "Idiopathic Calcification of the Cerebral Vessels." Thus originated the eponym "Fahr's disease," which may not be entirely pertinent since he reported a sporadic case in an adult rather than familial cases occurring in infancy and childhood. In 1935, Fritzsche[7] reported in detail his careful analysis of 3 siblings, the youngest of whom had skull roentgenograms at the age of 19 years, with the roentgenographic findings of symmetric calcifications in the basal ganglia and with clinical symptoms of mental retardation, dysarthria and convulsions. The autopsy findings in one of Fritzsche's cases were published in 1946 by Beyme.[2]

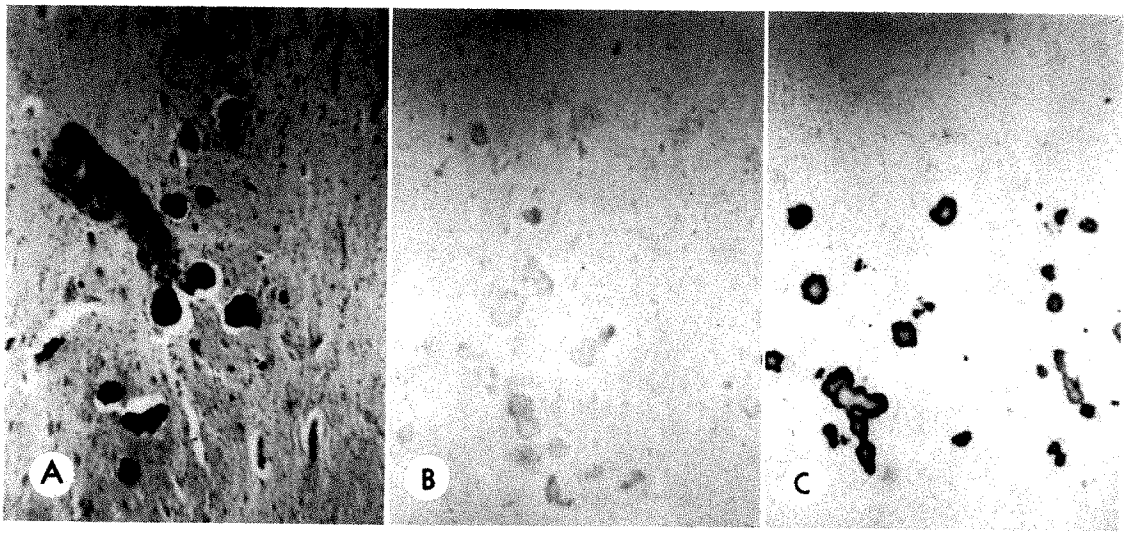


FIG. 1. (*A*) Dentate nucleus. Hematoxylin and eosin stain demonstrating dense mineral deposits. (*B*) Dentate nucleus. Calcium stain (von Kossa method); weakly positive. (*C*) Dentate nucleus. Iron stain (Prussian blue method); strongly positive.

Although the preceding papers have presented cases of idiopathic intracerebral calcification, none have included roentgenographic observations of patients below the age of 16 years. Nine cases in infancy and childhood have been reported as autopsied cases without roentgenographic studies, however.[11] The more recent literature, reviewed on patients with this disease, revealed only 5 other examples of children with skull roentgenograms showing intracerebral calcification. Two adolescents ($13\frac{1}{2}$ and 14 years) were reported by Eaton, Camp and Love[3] in 1939; 2 children (2 and 9 years) by Vasiliu[13] in 1940, and 1 infant (6 months) by Melchior *et al.*,[11] who in 1960 presented the largest series and an excellent review of the subject. Melchior and colleagues studied 2 families with the disease. In 1 family, 3 of 10 siblings, and in the other family, 2 of 4 siblings were affected. In each family, 1 patient died and underwent a thorough postmortem examination. The unaffected members were studied clinically and roentgenographically. The clinical symptoms and the physical, roentgenographic, and pathologic findings were similar to those in Fritzsche's and our cases.

PATHOLOGIC FINDINGS

The process of ferrugination and calcification in the vessels occurred in the subcortical centrum, basal ganglia, and the cerebellar dentate nucleus and its adjacent white matter. No similar ferrugination or calcification was present in the gray matter or elsewhere in the body. The ferrugination (Prussian blue staining method) was more marked microscopically than the calcification (von Kossa staining method) (Fig. 1, *A*, *B* and *C*). The process involved the terminal arterioles and venules in the areas where the iron and calcium were deposited; it is probable that this is secondary to a circulatory disturbance, resulting in local ischemia, edema, anoxia, necrosis and mummification with ferrugination and calcification.

ROENTGEN FINDINGS

The areas of ferrocalcinosis are widespread, irregular, punctate, and occasionally dust-like in appearance. The densest areas are frequently seen in the basal ganglia (Fig. 2 through 6). This roentgenographic appearance is not diagnostic but with the associated clinical findings, it should suggest the diagnosis.



Fig. 2. Lateral view of skull demonstrating dust-like periventricular calcification.

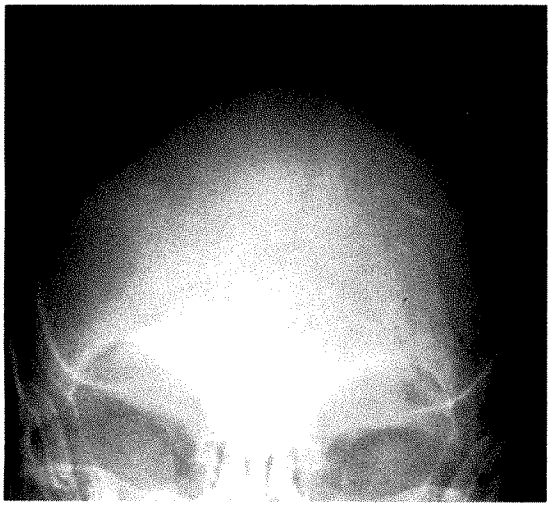


Fig. 4. Posteroanterior view of skull demonstrating calcification of the basal ganglia and periventricular structures.

Differential Diagnosis of Intracranial Calcification in Children

Physiologic calcifications occur in intracranial structures in children as in adults; however, calcification of the glomus of the choroid plexus and calcification of the pineal body are uncommon in children under the age of 10 years. Pineal calcification occurring under the age of 10 years suggests the possibility of a vestigial tumor of the pineal gland. Dural calcification is also uncommon in children with calcification of the petroclinoid ligaments, falx and dura usually considered to be of no clinical significance; however, occasionally calcification of the dura is evidence of hypervitaminosis D or hyperparathyroidism.

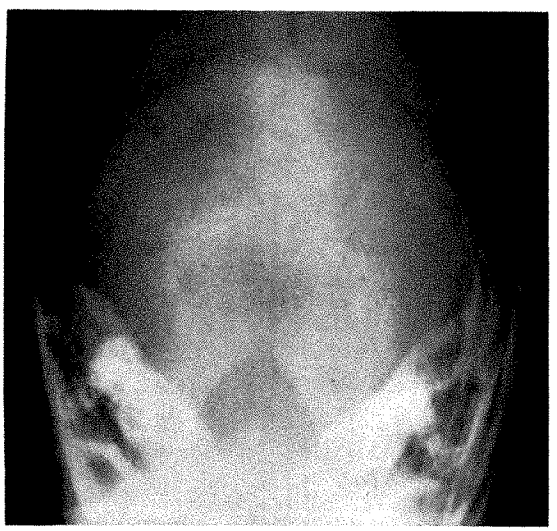


Fig. 3. Towne view of skull demonstrating dentate nucleus calcification.

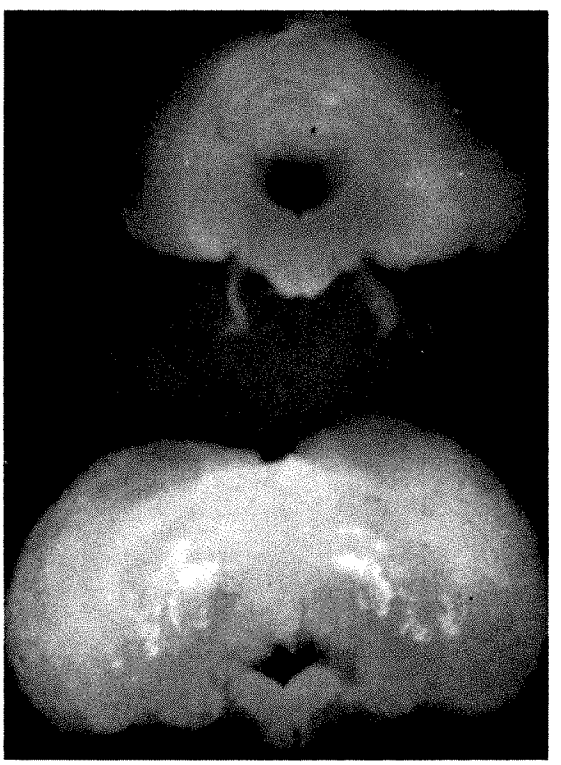


Fig. 5. Postmortem roentgenogram of coronal section through cerebellum demonstrating calcification of dentate nucleus and adjacent areas.



FIG. 6. Postmortem roentgenogram of coronal section through cerebrum demonstrating calcification of the basal ganglia and periventricular areas and hydrocephalus.

Pathologic intracranial calcifications (Table I) may occur in many disease states. As a general rule, atrophy secondary to infection, trauma, or hemorrhage is probably the commonest cause of intracranial calcification in children.

Parasitic Infestations. Toxoplasmosis is a relatively common cause. It represents a protozoan infestation which gives a positive Sabin dye and complement fixation test in the child and the mother. Microcephaly or hydrocephalus may occur secondary to the extensive encephalitic involvement of the brain by the widespread inflammatory process. Multiple focal areas of calcification of variable size scattered throughout the brain, particularly in the periventricular regions, are found roentgenographically.

Infectious Diseases. Cytomegalic inclusion disease is a virus infection that produces encephalitis, hepatosplenomegaly, petechiae, chorioretinitis and hemolytic anemia. The inclusion bodies associated with the viral infection are frequently found in the cells of the urinary sediment or in gastric washings. A virus culture may identify the causative virus. The calcifications usually are somewhat sheet-like and tend to outline lateral ventricles, but are not entirely specific. The appearance of the calcification can be similar to that of toxoplasmosis. Microcephaly or hydrocephalus may occur.

TABLE I

DISEASES WITH INTRACRANIAL CALCIFICATION

Parasitic: *Toxoplasmosis*, Cysticercosis, Echinococcosis, Trichinosis and Paragonimiasis

Infectious: *Cytomegalic Inclusion Disease*, Tuberculosis,* Abscesses,* Coccidioidomycosis, Generalized Herpes Simplex (Neonatal)[13] and Torulosis [12]

Vascular: *Sturge-Weber Disease*, *Aneurysms*,* Atherosclerosis, Angiomata and Arteriovenous Fistulas

Tuberous Sclerosis

Endocrine: Hyperparathyroidism,* Hypoparathyroidism,* and Pseudohypoparathyroidism, including Idiopathic Basal Ganglia Calcification

*Brain Tumors: Primary** (*including Craniopharyngioma*) and Metastatic

Toxic: Hypervitaminosis D,* Carbon Monoxide Poisoning, Lead Poisoning* and following Botulism and Tetanus

Teratomas:* Including Dermoids, Cholesteatomas and Lipomas

Subdural Hematoma,* *Intracranial Calcification following Hemorrhages from Various Causes* and Multiple Pulsating Leptomeningeal Cysts

Lissencephaly (Congenital Agyria)[15]

Idiopathic Familial Cerebrovascular Ferrocalcinosis (Fahr's Disease)

Those most prevalent are italicized.
* Potentially treatable disease.

Tuberculous meningitis has been cited by Lorber as a frequent cause of calcification, occurring in 48.7 per cent of 129 children who had tuberculous meningitis.[9] The calcification tends to localize about the base of the brain. The meninges are the site of the calcification in the majority of instances, while only a small percentage of the calcifications are in the brain substance.

Abscesses. Abscesses are a rare cause of intracranial calcification in childhood. They usually present with a neurologic manifestation of paralysis as a space occupying lesion often being associated with cyanotic congenital heart disease.

Generalized herpes simplex (neonatal)[6] and torulosis[12] may result, rarely, in intracranial calcification.

Vascular. The vascular calcification occurring in Sturge-Weber disease (encephalotrigeminal angiomatosis) reveals calcification in the parietal and occipital cortical areas associated with unilateral port wine stain of the face. The calcification appears as hairpin loops in these regions and is believed to be evidence of thrombosis of anomalous vascular channels on the surface of the brain.

Arteriovenous fistulas and other vascular malformations occasionally show calcification in childhood, but these are usually nonspecific.

Tuberous Sclerosis is associated with butterfly distribution of adenoma sebaceum on the face, mental retardation and convulsions, together with skeletal anomalies and renal cysts. Multiple oval or round calcifications in the lateral ventricular walls and basal ganglia may be seen. The intraventricular subependymal glial masses may be evident on pneumoencephalography and have the appearance of candle-gutterings.

Endocrine Diseases. In hyperparathyroidism, hypoparathyroidism, and pseudohypoparathyroidism, including idiopathic basal ganglia calcification, calcification may be seen in the basal ganglia, frequently with a symmetric distribution. The calcification in these diseases is more likely to be evident in older patients rather than in children. Calcification of the meninges and falx occasionally occurs in hyperparathyroidism.

Brain Tumors. Calcification in brain tumors other than that seen in craniopharyngioma is quite uncommon in childhood. In craniopharyngioma the presence of calcification in the suprasellar region associated with destruction of the sella turcica and clinical evidence of impairment of vision should strongly suggest the diagnosis. Calcification may occur in the slowly growing astrocytomas in the cerebellum and occasionally in ependymomas and choroid plexus papillomas. Calcification occurring in metastatic brain tumors is extremely rare in children except for metastases from osseous and chondral sarcomas.

Toxic States. Toxic states producing intracranial calcification are uncommon in children, the most notable of which is calcification of the meninges and falx in hypervitaminosis D, and in the child calcification in these structures should suggest the possibility of hypervitaminosis D.

Teratomas. Teratomas, including dermoids associated with congenital dermal sinus, may manifest themselves with calcification or possibly identifiable fat in the dermoid, but are more likely to be recognized roentgenographically by the presence of a midline skull defect representing the dermal sinus communicating with the brain. These occur most frequently in the region of the fourth ventricle. Occasionally, a lipoma may be identified by its central radiolucency surrounded by a thin rim of calcification.

Subdural Hematoma. Calcification following subdural hematomas may occur and the history in such instances would be of value in determining the cause of the calcification. The calcification in subdural hematomas tends to outline the area of the subdural hematoma with a fairly smooth curvilinear calcification adjacent to the inner table of the skull. Similarly, multiple

pulsating leptomeningeal cysts show curvilinear calcification.

Lissencephaly. In lissencephaly (congenital agyria) a small area of calcification lying in the anterior portion of the septum pellucidum is present, and dilatation of the ventricles is identifiable on pneumoencephalography. Extreme mental and physical retardation is clinically evident.[15]

SUMMARY

Three siblings with idiopathic familial cerebrovascular ferrocalcinosis (Fahr's disease) are reported. This is an uncommon cause of intracerebral calcification in children.

The differential diagnosis is discussed and a Table, listing the diseases associated with intracranial calcification, is presented.

Idiopathic familial cerebrovascular ferrocalcinosis apparently is not the result of an infectious process, endocrine disorder, or due to any known specific etiology. The disease is probably, as suggested by Fritzsche[7] and supported by Melchior *et al.*,[11] a genetically determined (autosomal recessive) metabolic disorder and/or vascular anomaly of a nature as yet unknown. It represents another cause of intracranial calcification in childhood.

D. P. Babbitt, M.D.
Department of Radiology
Milwaukee Children's Hospital
1700 West Wisconsin Avenue
Milwaukee, Wisconsin 53233

REFERENCES

1. BAMBERGER, H. Beobachtungen und Bemerkungen über Hirnkrankheiten. *Verhandl. phy. med. Gesellsch.* in Würzburg, 1855, *6*, 325.
2. BEYME, F. Über das Gehirn einer familiär Oligophrenen mit symmetrischen Kalkablagerungen, besonders in den Stammganglien. *Schweiz. Arch. Neurol. u. Psychiat.*, 1946, *56*, 161; 1946, *57*, 16.
3. EATON, L. M., CAMP, J. D., and LOVE, J. G. Symmetric cerebral calcification, particularly of basal ganglia, demonstrable roentgenographically. *Arch. Neurol. & Psychiat.*, 1939, *41*, 921–928.
4. ELISCHER, J. Über die Veränderungen im Gehirne bei Chorea minor. *Arch. path. Anat.*, 1875, *63*, 104.
5. FAHR, T. Idiopathische Verkalkung der Hirngefässe. *Zentralbl. allg. Path. u. Path. Anat.*, 1930, *50*, 129–133.
6. FARBER, S., and CRAIG, J. M. Clinical pathological conference. *J. Pediat.*, 1956, *48*, 800–811.
7. FRITZSCHE, R. Eine familiär auftretende Form von Oligophrenie mit röntgenologisch nachweisbaren symmetrischen Kalkablagerungen im Gehirn, besonders in den Stammganglien. *Schweiz. Arch. Neurol. u. Psychiat.*, 1935, *35*, 1–29.
8. GEYELIN, H. R., and PENFIELD, W. Cerebral calcification epilepsy. *Arch. Neurol. & Psychiat.*, 1929, *21*, 1020.
9. LORBER, J. Intracranial calcification following tuberculous meningitis in children. *Am. Rev. Tuberc.*, 1958, *78*, 38–61.
10. MALLORY, F. B. Contribution to study of calcareous concretions of brain. *J. Path. & Bact.*, 1896, *3*, 110.
11. MELCHIOR, J. C., BENDA, C. E., and YAKOVLEV, P. I. Familial idiopathic cerebral calcifications in childhood. *A.M.A. Am. J. Dis. Child.*, 1960, *99*, 787–803.
12. NEUHAUSER, E. B. D., and TUCKER, A. Roentgen changes produced by diffuse torulosis in newborn. AM. J. ROENTGENOL. & RAD. THERAPY, 1948, *58*, 805–815.
13. VASILIU, O. Sechs Fälle von symmetrischer intrazerebraler Kalkablagerung in den Stammganglien, verbunden mit epileptischen Anfällen und Geistesstörung, diagnostiziert mit Hilfe der Kraniographie und Encephalographie. *Wien. med. Wchnschr.*, 1940, *90*, 153.
14. VON HANSEMAN. Ein casuistischer Beitrag zur Verkalkung der Gehirngefässe. *Verhandl. Deutsch. Path. Gesellsch.*, 1899, *2*, 399.
15. WESENBERG, R. L., JUHL, J. H., and DALIBE, J. R. Radiolcgical findings in lissencephaly (congenital agyria). *Radiology*, 1966, *87*, 436–444.

VOL. 105, NO. 2

AUTOTOMOGRAPHY APPLIED TO THE PHARYNX AND DENS*

A SIMPLE WAND FOR THE TECHNIQUE

By EDWIN L. LAME, M.D., *and* THOMAS J. REDICK
COATESVILLE, PENNSYLVANIA

IN THE course of routine use of autotomography for lateral exposures of encephalograms, the clarity of demonstration of the naso- and oropharynx and of the odontoid process of the second cervical vertebra is apparent.[1,2]

It is not rare to have good delineation of the upper airway on a plain lateral skull roentgenogram (Fig. 1); however, if the pharynx is suspected of disease, a lateral autotomogram is even more valuable and is readily done (Fig. 2).

Similarly, chronic lesions of the dens, such as healing fracture, arthritis or malformation may be quite well shown by this technique (Fig. 3). Most acute in-



FIG. 2. Autotomogram (3 second exposure) improves definition and demonstrates the midline position of the lesion.

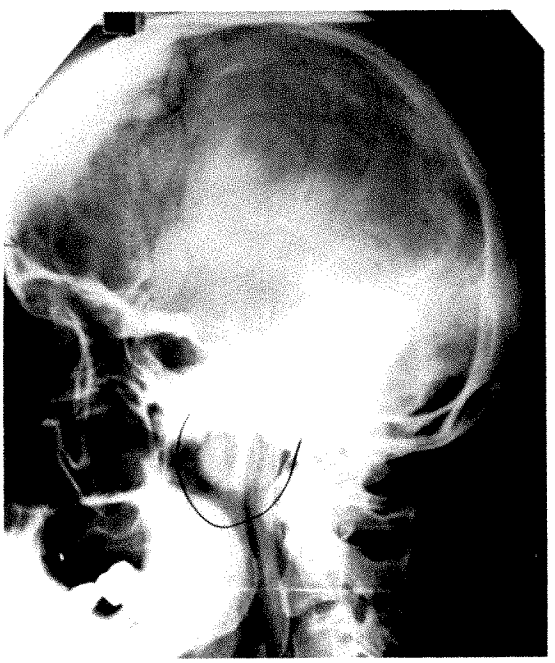


FIG. 1. Lateral projection of a skull roentgenogram showing a benign cystic polypoid hyperplasia of the mucosa of the nasopharynx.



FIG. 3. Increased density of autotomogram reveals odontoid process.

* From the Department of Radiology, Veterans Administration Hospital, Coatesville, Pennsylvania.

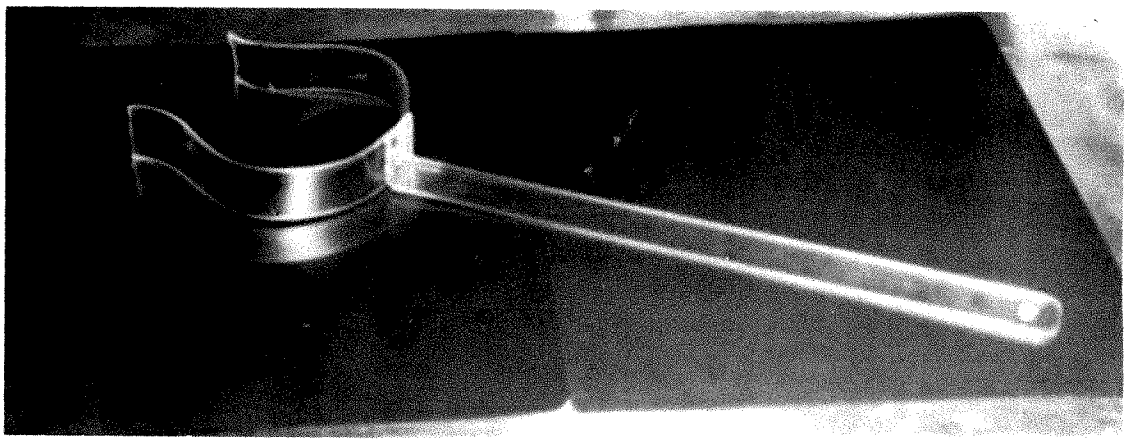


FIG. 4. Plexiglas wand $\frac{1}{8}$ inch thick, $1\frac{1}{2}$ inches wide with a curved headpiece 18 inches long, and a handle 18 inches long.

juries will not apply because of the attendant severe pain.

To simplify the technique of securing these exposures, a clear plexiglas wand has been constructed. The density of the 1/8 inch thick plastic does not interfere with the diagnostic quality on the roentgenogram but the 1/4 inch thickness does. The curve of the headpiece creates a satisfactory spring action to facilitate head rotation (Fig. 4 and 5).

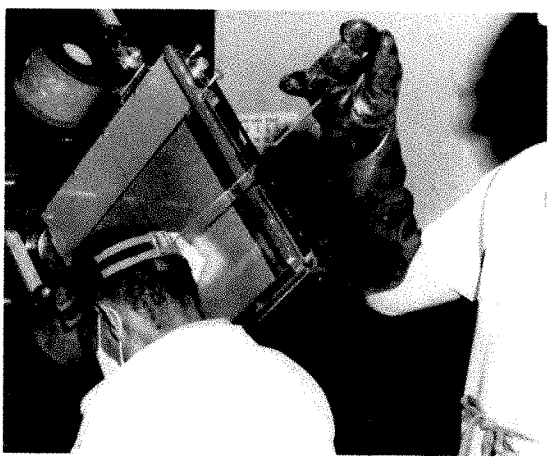


FIG. 5. One of the positions of patient during rotation by technician.

Edwin L. Lame, M.D.
Department of Radiology
Veterans Administration Hospital
Coatesville, Pennsylvania 19320

REFERENCES

1. SCHVARCZ, J. Autotomography of fourth ventricle and floor of third ventricle. *Acta radiol.*, 1959, *52*, 465–469.
2. VALLEBONA, A. Una modalità di tecnica par la dissociazione radiografica delle ombre applicata allo studio del cranio. *Radiol. med.*, 1930, *17*, 1090–1097.

Vol. 105, No. 2

ROENTGENOGRAPHIC EXAMINATION OF FORAMEN TRANSVERSARIUM OF AXIS*

PRACTICAL CONSIDERATIONS

By TRYGVE O. GABRIELSEN
ANN ARBOR, MICHIGAN

THE minimum diameter of the foramen transversarium of the axis is usually a fairly good indicator of the size of the corresponding vertebral artery.[2,4] The practical value and reliability of this observation will be discussed. The anatomy and roentgenographic examination of the foramen transversarium of the axis will also be described.

ANATOMY

The vertebral arteries ordinarily follow a vertical path through the foramina transversaria of the upper 6 cervical vertebrae. The only significant exception occurs at the level of the axis, where the cephalic portion of the canal turns almost straight laterally (Fig. 1, *A* and *B*). Although this part of the foramen has a quite variable orientation, it is approximately horizontal with respect to both an erect and supine posture. The deviation from this orientation is almost always in a dorsal direction.[2,4] The bony ring of the foramen transversarium of the axis is sometimes incomplete along its caudal and dorsal aspect.[2]

The vertebral artery favors a position at the periphery of the bend (along cephalic and dorsal margin) of the foramen transversarium of the axis. The accompanying venous plexus has a chiefly opposite location.[2,4]

The shape of the cephalic meatus of the canal varies considerably. On the average, the maximum diameter is about 1.0 mm. greater than the minimum diameter. The minimum diameter most often consists of an approximately ventral-dorsal diameter.[2,4] In 25 cadavers and 175 dried axis specimens, it ranged between 2.5 mm. and 7.5 mm., for an average of 5.0 mm.[2]



FIG. 1. Roentgenograms of dried axis specimen in (*A*) frontal and (*B*) axial projections. Walls of foramina transversaria (arrows) have been coated with barium. The canals in this specimen are quite asymmetric for size and shape.

ROENTGENOGRAPHIC EXAMINATION

The foramen transversarium of the axis cannot be clearly demonstrated on roentgenograms obtained in straight anteroposterior and lateral projections on the living patient, although the region of the cephalic meatus frequently can be identified. Laminagraphy in these planes, at least the frontal, is of little additional help.

However, the cephalic portion of the foramen transversarium of the axis can usually be seen quite easily in oblique roentgenograms of the cervical spine (Fig. 2). With an anteroposterior beam direction and the face of the patient turned to the right, the canal on the right side is shown.

* From the Department of Radiology, The University of Michigan Medical Center, Ann Arbor, Michigan.



FIG. 2. Oblique projection of cervical spine obtained with anteroposterior direction of beam and front of patient rotated to the right. The right foramen transversarium of the axis is clearly seen (arrow).

This foramen can also frequently be demonstrated on lateral skull roentgenograms obtained with the patient lying prone and the side of the face against the cassette (Fig. 3*A*; and 4*A*). Since the orientation of the cephalic part of the foramen transversarium of the axis is rather variable, it may be necessary to alter slightly the angle of projection for such standard views. A good evaluation of the canal may at times be most quickly obtained by performing laminagraphy in the position described for lateral skull examinations.

Although the foramen transversarium of the atlas can be seen on base views of the skull, this is of questionable value. According to Lindblom,[4] there is poor correlation between the size of the vertebral

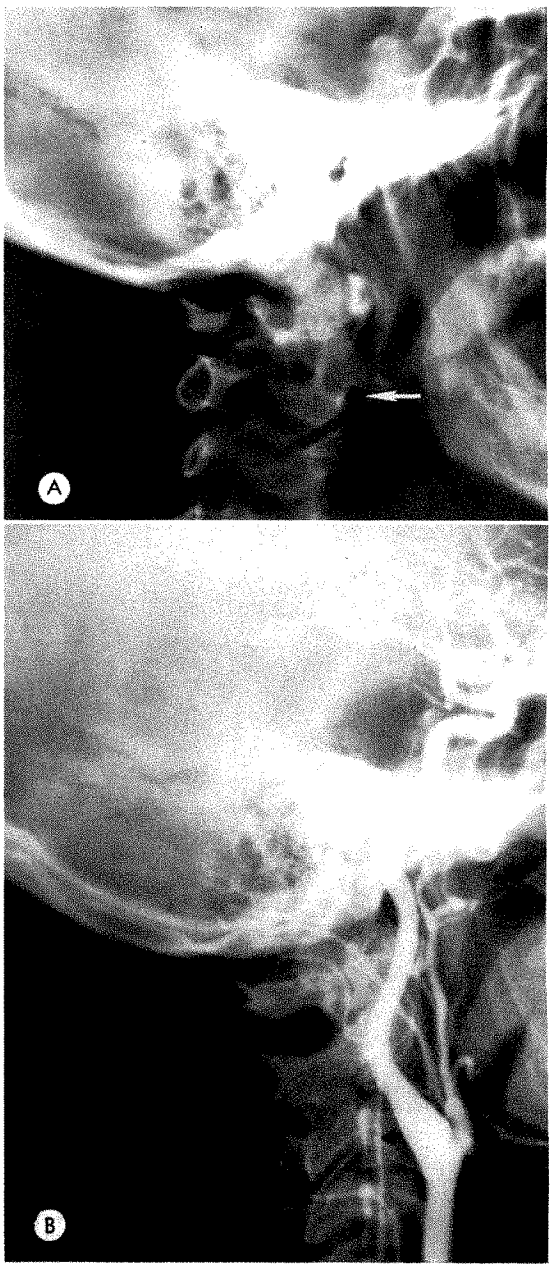


FIG. 3. (*A*) Lateral roentgenogram of the skull with patient lying prone and left side of face against cassette. Arrow points to small right foramen transversarium of axis. Minimum diameter is 3.5 mm. (*B*) Lateral projection of right retrograde brachial angiography. Lumen of right vertebral artery (arrow) is 1.5 mm. Measurements of artery and foramen have not been corrected for magnification.

artery and the size of its bony canal at this level.

DISCUSSION

In some clinical situations, it may be desirable to visualize both vertebral arteries. If vertebral angiography is done to investigate a lateralizing lesion in the posterior cranial fossa, it seems preferable to opacify the vertebral artery on the side of the lesion in order to demonstrate the ipsilateral posterior inferior cerebellar artery. However, technically good vertebral angiography on one side or the other may frequently suffice.

When the vertebral arteries are of quite unequal size and the larger one is injected selectively, there is often significant reflux of contrast material into the smaller one. Retrograde brachial angiography on the side of the larger rather than smaller vertebral artery also improves the chances for a technically satisfactory examination by decreasing the proportion of nonopaque blood in the basilar artery and its branches.

The smaller vertebral artery is found more frequently on the right than on the left side (Table 1). In 400 cadavers, Krayenbühl and Yaşargil[5] reported finding some cases with "very small" vertebral arteries bilaterally (0.75 per cent) or only on the left (4.5 per cent) or right (6.2 per cent). These percentage values correspond well with the experience of Stopford.[5] The present author found that 3 (12 per cent) of 25 cadavers had a vertebral artery lumen of 1.5 mm. diameter on one side.[2]

For such reasons, Yaşargil[6] always performs percutaneous vertebral angiography first on the left side. Selective vertebral arteriography by catheter techniques poses some different technical problems as well as definite advantages. It would seem helpful, especially in vertebral angiography with a direct percutaneous or retrograde brachial approach, if the radiologist, by a simple method, could be forewarned whenever one of the vertebral arteries is very small.

A small size of the foramen transversarium of the axis should serve as such a warning. For practical purposes, the minimum diameter of the cephalic part of this foramen is at least 1.0 mm. and most often 1.5 mm. to 2.0 mm. greater than the internal diameter of the corresponding vertebral artery at the same level.[2] Considerably greater discrepancy in size between the

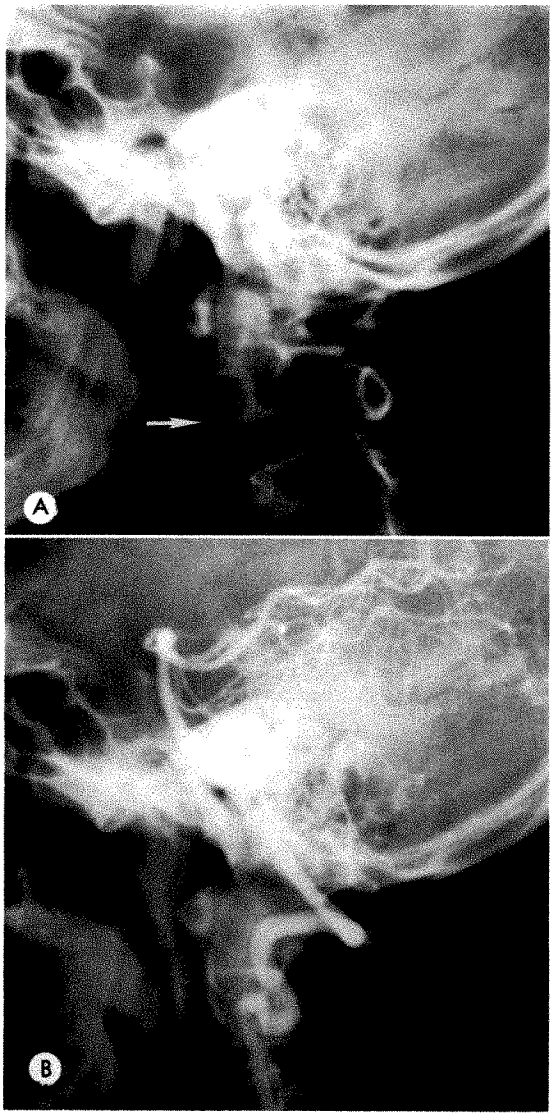


FIG. 4. Lateral roentgenogram of the skull with patient lying prone and right side of face against cassette. Arrow points to large left foramen transversarium of axis. Minimum diameter is 7.0 mm. (*B*) Lateral projection of left retrograde brachial angiography. Lumen of left vertebral artery (arrow) is 5.5 mm. Measurements of artery and foramen have not been corrected for magnification.

TABLE I

COMPARISON OF SIZE BETWEEN RIGHT AND LEFT SIDES FOR VERTEBRAL ARTERIES AND FORAMINA TRANSVERSARIA OF AXIS

Author	Material and Subject of Investigation	Findings		
		Right=Left (Per Cent)	Right>Left (Per Cent)	Left>Right (Per Cent)
Stopford[5]	Vertebral artery size in 150 cadavers	8	41	51
Krayenbühl and Yaşargil[3]	Vertebral artery size in 400 cadavers	26	32	42
Fields and Weibel[1]	Vertebral artery size in 1,200 bilateral vertebral arteriograms	34.1	20.7	45.2
Gabrielsen[2]	A. Measured lumen size of vertebral arteries in 25 cadavers	36	20	44
	B. Foramen transversarium of axis (minimum diameter measured) in 25 cadavers and 175 dried axis specimens	29.5	28	42.5

bony canal and the artery may exist, especially in the presence of vascular occlusive disease involving the vertebral artery.[2] Thus, there is the likelihood, but no guarantee, that a large vertebral artery will be present on the side of a large foramen transversarium of the axis. On the other hand, a small foramen can accommodate only a small artery. Proper attention paid to this fact might help to improve the technical quality and usefulness of vertebral angiography in some patients (Fig. 3, *A* and *B*; and 4, *A* and *B*).

SUMMARY

One can always predict that a small vertebral artery will be found at angiography whenever the foramen transversarium of the axis on the same side is small. The minimum diameter of the cephalic part of this canal is most often 1.5 mm. or 2.0 mm. greater than the internal diameter of the vertebral artery. Greater discrepancy in size may exist, especially in the presence of occlusive disease involving the vertebral artery.

The foramen transversarium of the axis can usually be seen in oblique projections of the cervical spine or on lateral roentgenograms of the skull obtained with the patient lying prone and the side of the face against the cassette. The pertinent anatomy is discussed.

Trygve O. Gabrielsen, M.D.
Department of Radiology
The University of Michigan Medical Center
Ann Arbor, Michigan

REFERENCES

1. FIELDS, W. S., and WEIBEL, J. Effects of vascular disorders on vestibular system. In: Neurological Aspects of Auditory and Vestibular Disorders. Edited by W. S. Fields, and B. R. Alford. Charles C Thomas, Publisher, Springfield, Ill., 1964, pp. 314–315.
2. GABRIELSEN, T. O. Size of vertebral artery and size of foramen transversarium of axis: an anatomic study. To be published.
3. KRAYENBÜHL, H., and YAŞARGIL, M. G. Die vaskulären Erkrankungen im Gebiete der Arteria Vertebralis und Arteria Basialis. Georg Thieme Verlag, Stuttgart, 1957, p. 39.
4. LINDBLOM, K. Roentgenographic study of vascular channels of skull, with special reference to intracranial tumors and arterio-venous aneurysms. *Acta radiol.*, 1936, Suppl. 30, pp. 18–21.
5. STOPFORD, J. S. B. Arteries of pons and medulla oblongata. *J. Anat. & Physiol.*, 1916, *50*, 131–164.
6. YAŞARGIL, M. G. Die Vertebralisangiographie: Ihre Bedeutung für die Diagnose der Tumoren. *Acta neurochir.*, 1962, Suppl. 9, 7–8.

Vol. 105, No. 2

CALCIFICATION OF THE POSTERIOR LONGITUDINAL LIGAMENT: A CAUSE OF CERVICAL MYELOPATHY*

By HIDEYO MINAGI, M.D., *and* ARTHUR T. GRONNER, M.D.
SAN FRANCISCO, CALIFORNIA

OSTEOPHYTIC encroachment on the spinal canal or neural foramina may be a cause of compression of the spinal cord or nerve roots.[1,6,8] Hinck and Sachdev[3] have pointed out that even relatively small cervical osteophytes may compress the cord when the sagittal diameter of the spinal canal is deficient on a developmental basis. More recently, Onji *et al.*[5] have attributed compression of the extradural cervical cord in 18 Japanese patients with myelopathy to encroachment by a calcified posterior longitudinal ligament. Correlation of the calcification with the usual roentgenographic signs of spondylosis was not apparent.

Although these authors cited several references to this entity in the Japanese literature, we could find no similar cases described in the English language literature.

A report is presented of 2 patients in whom roentgenograms of the cervical spine appeared identical to those described by Onji *et al.*[5]

REPORT OF CASES

CASE 1. This 57 year old white male was seen in the Out-Patient Department of the University of California Medical Center, San Francisco, on January 12, 1967 because of neurologic difficulties of long duration. Ten years previously the patient had first noted weakness and numbness in the left arm and leg. These complaints increased during the next several years, accompanied by progressive clumsiness and difficulty in walking. In the 2 years preceding examination, numbness and difficulty in the use of the right hand increased and handwriting became progressively illegible. A progressive disturbance in bladder function with urgency and incontinence was also noted.

Roentgenograms of the skull and a carotid arteriogram obtained elsewhere in 1960 were reported as unremarkable. Several electroencephalograms during this period were also interpreted as being normal. A pneumoencephalogram in 1962 and myelogram in 1964 showed no abnormality.

In October 1966, the patient was admitted elsewhere for the same complaints. On physical examination at that hospital clinical evidence of both spinal cord and nerve root compression was demonstrated at the levels of the fifth to seventh cervical vertebrae. Roentgenograms of the cervical spine reportedly showed severe spondylosis, and cervical myelography demonstrated multiple levels of compression. A laminectomy of the third through the seventh cervical vertebrae was performed. At surgery it was noted that the dura did not pulsate. The intradural space was not explored. No improvement was noted after the operation and the weakness in the legs and arms became more marked.

Physical examination on January 11, 1967 disclosed fasciculation in both forearms and hands with wasting of the muscles of both hands, slightly more on the left. Marked weakness of the triceps and biceps was also greater on the left. The right side of the body was almost anesthetic and hypoesthesia was noted on the left. Sense of position was poor in both feet and absent in the hands. Vibratory sense was poor in the lower extremities and absent in the upper. Bilateral unsustained ankle clonus and a bilateral Babinski sign were noted.

Roentgenograms of the cervical spine, including tomograms, demonstrated a calcified structure 5 cm. in length within the cervical spinal canal, extending from the second to the fifth cervical vertebrae (Fig. 1, *A* and *B*). At the level of the third cervical vertebrae, the calcified structure had reduced the sagittal diameter of the spinal canal by one-half. On review of previous outside roentgenograms, this calcification was observed on those of 1961,

* From the Departments of Radiology, University of California School of Medicine, and Children's Hospital and Adult Medical Center, San Francisco, California.

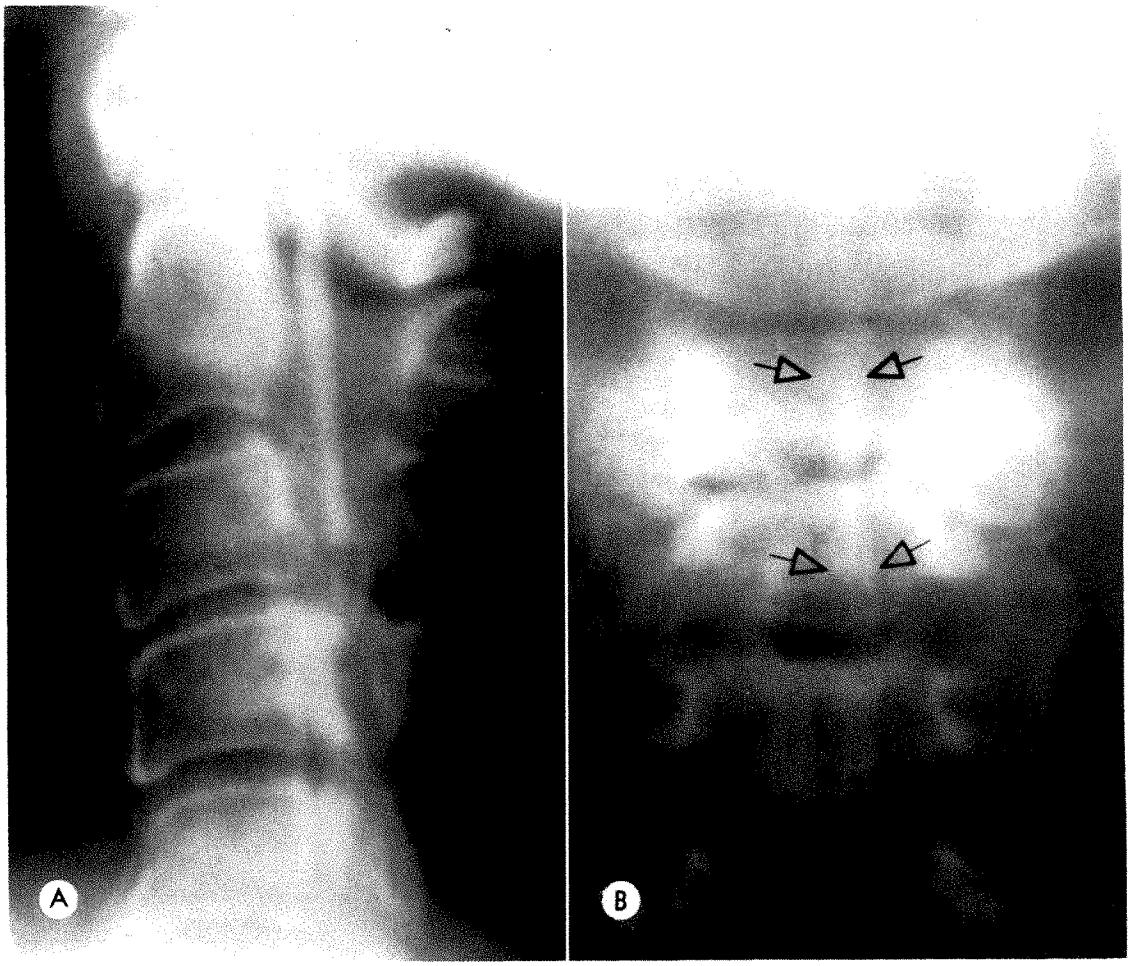


FIG. 1. Case I. (*A*) Lateral and (*B*) frontal tomograms demonstrate calcification of the posterior longitudinal ligament. The calcified ligament is in close apposition to the posterior aspects of the fourth and fifth cervical bodies, but is slightly separated from the bodies of the second and third cervical vertebrae (arrows).

which were the earliest available (Fig. 2). No progression in its extent was noted. The myelogram obtained prior to laminectomy in 1966 (Fig. 3) demonstrated contrast material projected over the calcified ligament.

CASE II. This 75 year old white woman was admitted to the Children's Hospital and Adult Medical Center, San Francisco, in 1966 for investigation of chest pain and symptoms of cerebral vascular insufficiency. There was no history of dizziness, head trauma, or other neurologic difficulty, although she had complained of left-sided headaches since childhood. An electroencephalogram showed ill defined focal dysfunction on the left side, compatible with circulatory disturbance. She was discharged from the hospital without treatment.

In December 1967, the patient was readmitted complaining that diminution in memory had been noted for 6 months. Neurologic examination at that time revealed exaggerated deep tendon reflexes in the biceps, triceps, wrists, and knees. The plantar reflexes were normal, as were the motor and sensory tests. Examination of the cranial nerves revealed no abnormality. Arteriographic studies disclosed arteriosclerotic narrowing at the origin of the right internal carotid and right vertebral arteries, and occlusion of the left vertebral artery. Observed incidentally on the arteriograms was a 5 cm. bony structure within the spinal canal, immediately posterior to the bodies of the second and third cervical ver-

tebrae (Fig. 4). In retrospect, this structure had been present on a lateral cervical esophagogram in 1958 (Fig. 5). Review of a stereoscopic lateral roentgenogram of the skull, obtained in 1960, confirmed its presence within the spinal canal in the midline. No change in the extent of the ossification was apparent.

DISCUSSION

Except for the reports by Onji and Akiyama[4] and Onji *et al.*,[5] we have been unable to find any reference to the entity of posterior longitudinal ligament calcification in the English language literature. Cloward,[2] in a personal communication to Onji *et al.*,[5] stated that he could find no such calcification in a review of more than 1,000 roentgenograms of patients with cervical spine disease. Nearly half of these patients had been of Japanese ancestry, living in Hawaii.

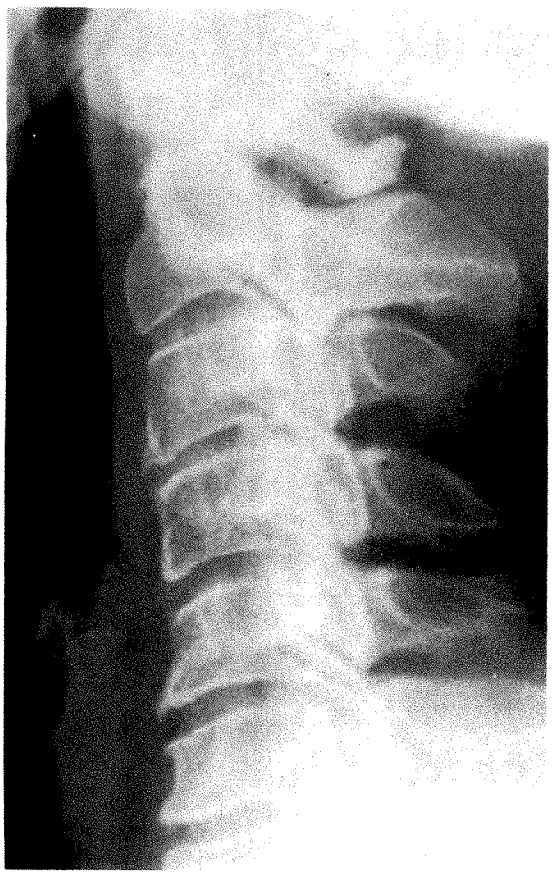


FIG. 2. Case 1. A lateral roentgenogram of the cervical spine in 1961 shows that the extent of the calcification is the same as in 1967 (Fig. 1).

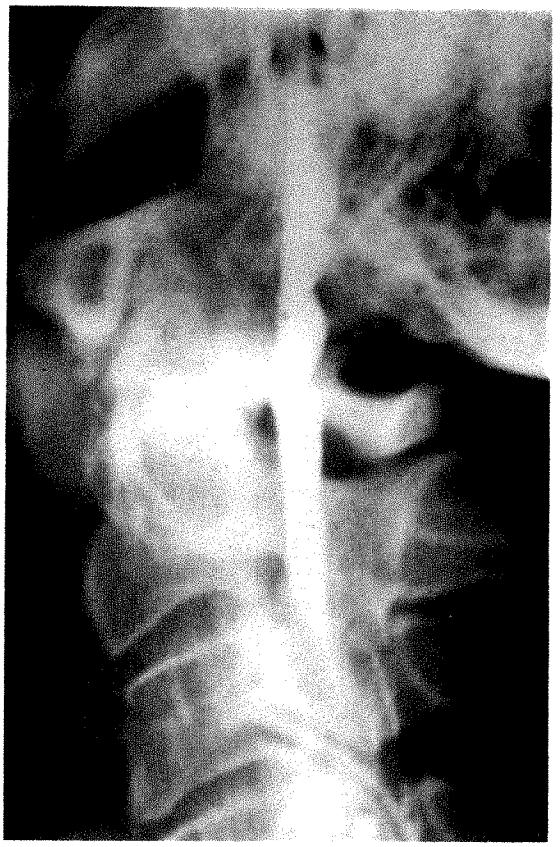


FIG. 3. Case 1. Myelogram preceding laminectomy in 1966 shows the calcified ligament to be obscured by overlying contrast material.

Onji *et al.*[5] reported a 1.7 per cent incidence of calcification of the cervical posterior longitudinal ligament among their Japanese patients with cervical spine disorders. Our 2 cases are apparently the first non-Japanese patients in whom this disorder is described. The calcified ligament probably has been either overlooked, or been mistaken for posterior osteophytic change associated with cervical spondylosis.

Terayama *et al.*[7] described the necropsy findings in a patient with ossification of the posterior longitudinal ligament, who died shortly after surgery. At some segments, a gap consisting of loose vascular connective tissue was present between the posterior margin of the cervical vertebral body and



FIG. 4. Case II. Preliminary roentgenogram prior to carotid arteriography. The calcified posterior longitudinal ligament lies posterior to the bodies of the second and third cervical vertebrae.

the ossified structure. At other segments the ossification merged into the posterior wall of the vertebral body. Overlying the ossification was a thin layer of fibrous tissue, interpreted as part of the posterior longitudinal ligament. Histologically, the ossification consisted of lamellar bone containing cavities, similar in appearance to bone marrow.

The calcified or ossified posterior longitudinal ligament in Case II apparently did not cause symptoms. Although the deep tendon reflexes of this patient were reportedly exaggerated, the plantar responses were normal. Conversely, Case I, with a long history of symptoms referable to cervical myelopathy was similar to the patients described by Onji *et al.*[5]

The diagnosis in other patients with cervical myelopathy from calcification of the longitudinal ligament has undoubtedly been missed in the past. Since laminectomy resulted in subjective and objective improvement in most of the patients so treated by Onji *et al.*,[5] calcification of the posterior longitudinal ligament should be sought in patients with signs or symptoms of cervical spinal cord disease.

SUMMARY

Calcification of the posterior longitudinal ligament has been reported recently as a cause of cervical myelopathy in Japanese

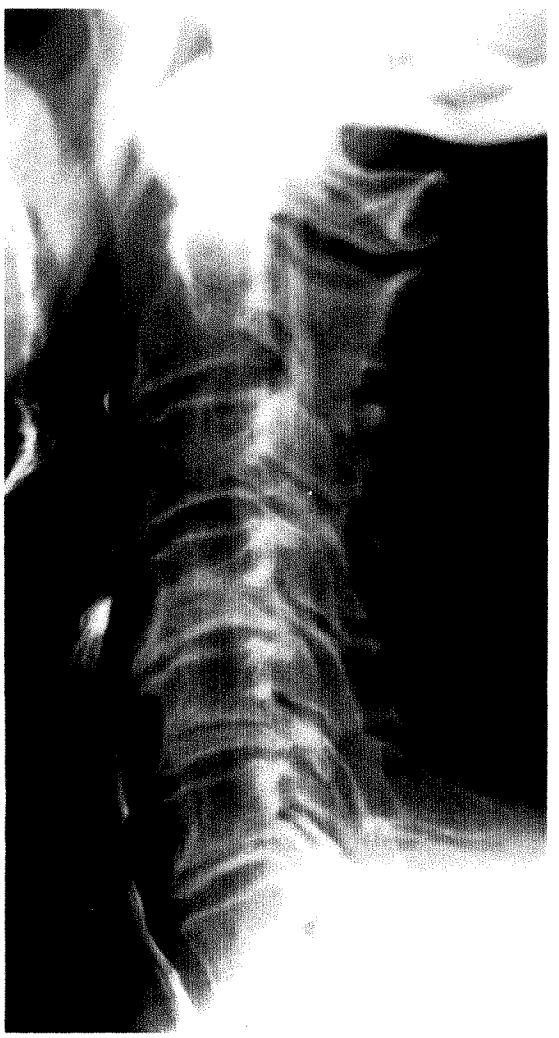


FIG. 5. Case II. The calcified ligament was present as indicated on a lateral esophagogram in 1958, but was overlooked. The extent of the calcification is the same as in 1967 (Fig. 4).

patients. The roentgenologic and clinical changes in 2 Caucasian patients with such calcification are presented and discussed.

A search for ligamentous calcifications is advised in patients with signs or symptoms of cervical spinal cord disease.

Hideyo Minagi, M.D.
Department of Radiology
University of California
San Francisco Medical Center
San Francisco, California 94122

REFERENCES

1. Brain, W. R., Northfield, D., and Wilkinson, M. Neurological manifestations of cervical spondylosis. *Brain*, 1952, *75*, 187–225.
2. Cloward, R. Personal communication. Quoted by Y. Onji, *et al.*[5]
3. Hinck, V. C., and Sachdev, N. S. Developmental stenosis of cervical spinal canal. *Brain*, 1966, *89*, 27–36.
4. Onji, Y., and Akiyama, H. Surgical treatment of cervical spondylotic myelopathy. *J. West. Pac. Orthop. A.*, 1965, *2*, 103–108.
5. Onji, Y., Akiyama, H., Shimomura, Y., Ono, K., Hukuda, S., and Mizuno, S. Posterior paravertebral ossification causing cervical myelopathy: report of eighteen cases. *J. Bone & Joint Surg.*, 1967, *49A*, 1314–1328.
6. Payne, E. E., and Spillane, J. D. Cervical spine: an anatomico-pathological study of 70 specimens (using special technique) with particular reference to problem of cervical spondylosis. *Brain*, 1957, *80*, 571–596.
7. Terayama, K., Maruyama, S., Miyashita, R., and Kinoshita, M. Calcification of cervical longitudinal posterior ligament. Quoted by Y. Onji, *et al.*[5]
8. Wilkinson, M. Morbid anatomy of cervical spondylosis and myelopathy. *Brain*, 1960, *83*, 589–617.

ROENTGENOGRAPHIC CORRELATIONS IN CERVICAL SPONDYLOSIS*

By H. A. WILKINSON, M.D., M. L. LEMAY, M.D., *and* E. J. FERRIS, M.D.
BOSTON, MASSACHUSETTS

CERVICAL spondylosis is a progressive and disabling disease of later life. Pathologically, it begins as a degeneration in the lower cervical intervertebral disks, with later development of bony hypertrophic changes along the margins of the affected interspaces.

Roentgenographically, considerable disagreement exists as to the clinical significance of the changes seen on plain roentgenograms and myelograms in cervical spondylosis. Likewise there is little agreement concerning the correlation between the findings on plain roentgenography and the findings on myelography. To study these areas of uncertainty, the authors have reviewed the roentgenographic findings of a series of 54 patients with the clinically accepted diagnosis of cervical spondylosis who were seen between 1963 and 1965 at the Boston Veterans Administration Hospital. Other patients, in whom plain roentgenographic and myelographic studies were inadequate for the purpose of this study, have been excluded.

METHOD

A series of measurements have been made on plain roentgenograms of the cervical spine and on cervical myelograms. These measurements have been cross-correlated and statistically analyzed in an effort to evaluate various anatomic features and the relationship of various features as demonstrated on plain roentgenographic and myelographic studies. The 4 interspaces between C3 and C7 were studied both by lateral and oblique plain roentgenography and by cervical myelography. All plain roentgenographic measurements were made from a standard 72 inch tube-patient distance. In lateral views the pre-existing sagittal diameter of the spinal canal was measured from the midposterior body of each vertebra to the nearest point on the corresponding lamina, as recommended by Payne and Spillane.[7] The height of posterior interbody spurs and the "absolute anteroposterior" diameter of the cervical spinal canal were measured from that point where the interspace was transected by a line drawn between the center of the posterior surfaces of the 2 adjacent vertebral bodies. The posterior extremity of the "absolute anteroposterior" diameter of the canal was taken to be the closest point on the midline dorsal laminae to the particular interspace. The degree of foraminal encroachment seen on oblique plain roentgenograms was given the following semiquantitative valuations: severe, moderate, mild or none.

All myelograms included both posteroanterior and lateral projections of the lower cervical region. All measurements were made on roentgenograms exposed at a standard 40 inch tube-patient distance. The degree of transverse interruption of the column of contrast medium on the posteroanterior studies (*i.e.*, the severity of "myelographic bars") was semiquantitated as: severe, moderate, mild or none. Measurements were also made on the posteroanterior roentgenograms at each vertebral level of the interpedicular distance ("canal width") and of the width of the cord shadow within the column of contrast medium ("cord width"). On roentgenograms taken in the lateral projection, measurements were made at each vertebral level from the anterior limit of the cord shadow within the column of contrast medium to the nearest point on the overlying laminae to give a rough approximation of "sagittal cord diameter" (Fig. 1).

* From the Departments of Neurosurgery and Radiology, Boston Veterans Administration Hospital and Boston City Hospital, Boston, Massachusetts.

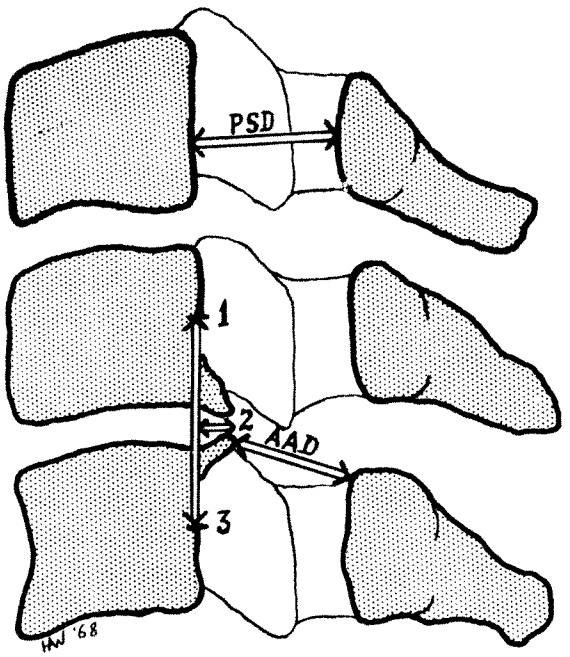


Fig. 1. Measurements on plain lateral roentgenograms. PSD = Pre-existing sagittal diameter of spinal canal. AAD = Absolute anteroposterior diameter of spinal canal. The line from 1 to 3 forms the baseline from which the height of posterior spurs was measured (2).

This posterior bone landmark was chosen for measurement since all myelograms were obtained with the patient prone, so that the posterior limit of the cord shadow was rarely demonstrated.

Clinically the patients were divided into 4 groups: (1) Those patients in group 1, who complained of neck and/or arm pain only, but displayed no obvious neurologic deficit (9 patients); (2 and 3) those patients in groups 2 and 3, who displayed essentially pure objective clinical findings of radiculopathy (25 patients) or myelopathy (6 patients), respectively—with or without pain; and (4) those patients in group 4, who had a mixture of radicular and myelopathic findings (14 patients). A detailed study of clinical-roentgenographic correlations is contained in a second report.[9]

Table II

Average "absolute" anteroposterior diameter of spinal canal

Clinical Groups	C3–4	C4–5	C5–6	C6–7
1. Pain	—	—	—	—
2. Radicular	15.5	15.7	14.8	14.9
3. Myelopathic	10.8	13.1	12.2	—
4. Mixed	12.5	13.1	12.6	13.8

Results

Average measurements of "pre-existing" sagittal canal diameter, "absolute" anteroposterior canal diameter, cord width and canal width are demonstrated in Tables I–IV, and are in close agreement with previously reported measurements.[1–6]

Roentgen Correlations

"Transverse bars" on myelography are assumed to represent anterior encroachment upon the column of contrast medium by posterior interbody osteophytes (or "spurs," as seen on lateral cervical roentgenograms). In this study the height of posterior interbody spurs seen on plain roentgenograms correlated almost perfectly (correlation coefficient "r" = 0.989) with the severity of transverse bars demonstrated on myelography (Table V). No patient with large posterior spurs demonstrated on plain roentgenograms failed to display prominent transverse filling defects

Table I

Average "pre-existing" sagittal diameter of canal

Clinical Groups	C1	C2	C3	C4	C5	C6	C7
1. Pain	22.5	19.1	17.1	16.3	16.4	16.4	16.4
2. Radicular	19.9	18.5	16.4	14.6	15.1	14.9	14.9
3. Myelopathic	19.8	17.3	13.5	13.7	13.7	14.0	14.0
4. Mixed	20.7	16.9	14.3	13.2	12.5	13.2	13.2

TABLE III

AVERAGE WIDTH OF SPINAL CORD

Clinical Groups	C3–4	C4–5	C5–6	C6–7
1. Pain	17.4	17.9	18.1	17.6
2. Radicular	19.3	18.2	18.4	17.5
3. Myelopathic	18.3	16.0	15.3	15.0
4. Mixed	18.1	17.1	17.9	16.8

on myelography. Occasional patients with no spurs, or with tiny spurs, were found to have sizable myelographic bars, presumably because of noncalcified posterior protrusions. These severe defects would have been underrated by reliance on plain roentgenograms alone in no less than 23 interspaces included in the present study.

Foraminal encroachment is generally presumed to result from lateral extensions of posterior interbody spurs. In this study, the severity of foraminal encroachment seen on oblique plain roentgenograms correlated moderately well ($r=0.530$) with the severity of posterior interbody spurs seen at corresponding interspaces on lateral plain roentgenograms and correlated slightly less well ($r=0.402$) with the severity of myelographically demonstrated transverse bars. Not unexpectedly the greatest discrepancies occurred in a small group of patients in whom marked transverse bars on myelography were associated neither with large posterior interbody spurs nor with significant foraminal encroachment as demonstrated on plain roentgenograms, presumably indicating the presence of noncalcified posterior protrusions, or "soft disks." However, only at one interspace in one patient were both a marked transverse bar and a large posterior interbody spur seen with no significant foraminal encroachment, thus confirming a high degree of correlation of foraminal encroachment in the presence of significant calcified posterior osetophytic spurs.

In an attempt to demonstrate flattening of the spinal cord itself against underlying posterior interbody spurs, measurements of spinal cord width were correlated with the height of posterior interbody spurs seen on plain roentgenograms and with the severity of myelographically demonstrated transverse bars. In neither instance was a reliable degree of correlation found ($r=0.218$ and 0.320, respectively). Khilnani and Wolf[5] have suggested that a more accurate index of cord flattening is a demonstrable increase in width at the affected level over the width of adjacent segmental levels—or an increase in width at a given level relative to the interpedicular canal width. They felt that a relative increase in cord width greater than 3 mm. or an increase in ratio of cord/canal width greater than 80 per cent "should be considered suspicious of an abnormality." In this study cord width was found to correlate poorly with canal width ($r=0.103$). Accordingly, both the absolute cord width and the relative increase in cord width were compared to the severity of posterior interbody spurs and myelographic bars. No reliable degree of correlation was found for either measurement of cord width with spur size ($r=0.218$ and 0.166, respectively), and only modest correlation was found with myelographically demonstrated transverse bars ($r=0.320$ and 0.353, respectively).

Since much importance has been placed on the significance of a diminished sagittal spinal canal diameter in cervical spondylosis, we also compared our measurements of canal sagittal diameter and canal width. We hoped thereby to distinguish between a generalized decrease in canal size and a specific canal flattening. In this instance a

TABLE IV

AVERAGE WIDTH OF SPINAL CANAL

Clinical Groups	C3–4	C4–5	C5–6	C6–7
1. Pain	27.0	26.0	26.2	26.0
2. Radicular	25.1	25.8	26.0	25.4
3. Myelopathic	—	—	—	—
4. Mixed	23.6	23.9	24.4	24.2

TABLE V

ROENTGENOGRAPHIC CORRELATION

A. Relationships of Other Roentgenographic Measurements to Height of Posterior Spurs
No. of Measurements/Per Cent

	Smaller than Expected	Correspondingly Equal in Size	Larger than Expected	Correlation Coefficient*
Foraminal encroachment	2 1.4	125 85	20 13.6	$r=0.530$ $P=10^{-10}$
Width of spinal cord	17 10	129 76	23 14	$r=0.218$ $P=0.00004$
Change in cord width	25 14	138† 79	11 7	$r=0.166$ $P=0.03$

B. Relationships of Other Roentgenographic Measurements to Severity of Myelographic Bars
No. of Measurements/Per Cent

	Smaller than Expected	Correspondingly Equal in Size	Larger than Expected	Correlation Coefficient*
Foraminal encroachment	27 19	104 73	12 8	$r=0.402$ $P=2\times10^{-6}$
Height of posterior spurs	6 3	181 89	17 8	$r=0.989$ P=1/Inf.
Width of spinal cord	14 8	116 66	47 26	$r=0.320$ $P=0.00004$
Change in cord width	50 32	103 66	4 2	$r=0.353$ $P=0.00004$

C. Relationships of Other Roentgenographic Measurements to Width of Spinal Canal
No. of Measurements/Per Cent

	Smaller than Expected	Correspondingly Equal in Size	Larger than Expected	Correlation Coefficient*
Width of spinal cord	52 31	92 55	22 14	$r=0.103$ $P=0.16$
Width of sagittal canal	14 8	131 79	21 13	$r=0.407$ $P=2\times10^{-8}$

* Calculations of correlation coefficient (r) utilized the method for grouped data, with a minimum 20 space grid. A perfect and linear correlation would yield a coefficient of 1.000, while a coefficient of zero would denote a complete lack of correlation. Probability factor (P) for these correlations is considered significant if less than 0.05. The categories here depicted represent oversimplifications of complex data, and are presented chiefly for illustration of statistical trends.

† Of this group, 102 showed neither significant posterior spurs nor change in cord width, thus unbalancing the data and lessening its reliability.

moderately good correlation was found ($r=0.407$), thereby emphasizing a generalized decrease in canal size affecting both sagittal and transverse diameters.

CONCLUSION

In the present series of patients with the clinical diagnosis of cervical spondylosis, good correlations have been demonstrated

between the findings on lateral and oblique plain roentgenograms of the cervical spine and the findings on cervical myelography. With such good correlations it might seem reasonable to discontinue the more arduous procedure of myelography and to rely instead entirely on plain roentgenograms, a move which Taylor[8] has indeed endorsed. One feature of the present study, however, argues strongly in favor of myelography: in most instances in which correlation was imperfect the patient was found to have more significant defects on myelography than on plain roentgenograms.

SUMMARY

The authors have reviewed and correlated the plain roentgenograms and myelograms of a series of 54 patients with cervical spondylosis in an effort to clarify the considerable ambiguities which exist concerning the significance of the roentgenographic findings in this disorder. The results were as follows:

1. Transverse bars on myelography correlated almost perfectly with posterior interbody spurs on plain roentgenograms. Occasional patients were found to have more significant defects on myelography than on plain roentgenograms, but the reverse situation was not encountered.

2. Foraminal encroachment was found to correlate well with the presence of significant posterior interbody spurs. This was felt to support the presumption that foraminal encroachment likely develops as lateral extensions of posterior interbody spurs.

3. No reliable degree of correlation was found between various measures of spinal cord widening on myelography, either with measurements of posterior interbody spurs or with severity of transverse bars.

4. Diminished sagittal spinal canal diameter, a well-recognized concomitant of cervical spondylosis, was found to occur as one dimension of a generalized decrease in canal size affecting both sagittal and transverse diameters.

H. A. Wilkinson, M.D.
Neurosurgical Service
Sears Building, Third Floor
Boston City Hospital
818 Harrison Avenue
Boston, Massachusetts 02118

REFERENCES

1. BOIJSEN, E. Cervical spinal canal in intraspinal expansive processes. *Acta radiol.*, 1954, *42*, 101–115
2. BRADSHAW, P. Some aspects of cervical spondylosis. *Quart. J. Med.*, 1957, *26*, 177–208.
3. FRIEDENBERG, A. B., EDEIKER, J., SPENCER, H. N., and TOLENTINO, S. C. Degenerative changes in cervical spine. *J. Bone & Joint Surg.*, 1959, *41A*, 61–70.
4. KEEGAN, J. J. Cause of dissociated motor loss in upper extremity with cervical spondylosis: case report. *J. Neurosurg.*, 1965, *23*, 528–526.
5. KHILNANI, M. T., and WOLF, B. S. Transverse diameter of cervical spinal cord on pantopaque myelography. *J. Neurosurg.*, 1963, *20*, 660–664.
6. NUGENT, G. R. Clinicopathologic correlations in cervical spondylosis. *Neurology*, 1959, *9*, 273–281.
7. PAYNE, E. E., and SPILLANE, J. D. Cervical spine: anatomico-pathological study of 70 specimens (using special technique) with particular reference to problem of cervical spondylosis. *Brain*, 1957, *80*, 571–596.
8. TAYLOR, A. R. Vascular factors in myelopathy associated with cervical spondylosis. *Neurology*, 1964, *14*, 62–68.
9. WILKINSON, H. A., LEMAY, M. L., and FERRIS, E. J. Clinical-radiographic correlations in cervical spondylosis: approach to pathophysiology. To be published.

VOL. 105, NO. 2

THE NEUROLOGIC COMPLICATIONS OF PAGET'S DISEASE IN THE CERVICAL SPINE*

By FRIEDA FELDMAN, M.D.,† *and* WILLIAM B. SEAMAN, M.D.‡
NEW YORK, NEW YORK

THE cervical spine is rarely affected by Paget's disease and when it is, the roentgen appearance frequently differs from that seen in other parts of the skeleton. The purpose of this report is to describe the peculiarities of the roentgen appearance of this disease in the cervical spine and to emphasize the frequency and seriousness of its neurologic complications.

INCIDENCE

According to a recent report of 2 patients by Janetos,[8] only 26 cases had previously been described.[2,3,4,6,10,11,13,16,17,18] He did not include the 10 examples noted in Schmorl's study of 69 autopsied cases.[12] Of 116 cases reviewed by Gutman and Kasabach,[4] the cervical spine was examined in 46, 5 of which showed evidence of disease without apparent symptoms. Dickson *et al.*[2] found cervical spine involvement in 6 of 367 cases and listed it as thirteenth in order of frequency of involvement.

Schwarz and Reback[13] reporting 40 cases of thoracic spine involvement from the Columbia–Presbyterian Medical Center in 1939, included 3 patients in whom the cervical spine was also affected.

We reviewed over 500 cases of Paget's disease seen at the Columbia–Presbyterian Medical Center from 1953 to 1966 and found 46 in whom the cervical spine was examined. However, the upper portion of the cervical spine was visualized in roentgenograms of the skull in 122 additional patients. Eleven examples of cervical spine involvement were found which constitute the basis of this report (Tables I, II and III). Three patients had evidence of spinal cord compression confirmed by operative or autopsy findings, while a fourth is experiencing symptoms probably resulting from subluxation and mild compression.

CLINICAL FEATURES

The most striking clinical feature is the frequency of neurologic symptoms, which was the primary complaint in 4 patients in this group. These are due to encroachment on the spinal canal or intervertebral foramina as a consequence of vertebral compression, bone overgrowth or both. It is also possible that symptoms may arise from interference with the blood supply to the spinal cord.[9]

REPORT OF CASES

CASE I. S.M., a 42 year old white male, complained of numbness and weakness of both upper and lower extremities of 4–6 months' duration. Weakness of the hands had been present for 1 year. Physical examination revealed weakness of all extremities, more marked on the left, hyperreflexia, and decreased position and vibratory sense. The Babinski response was positive bilaterally. The alkaline phosphatase level was 24 King-Armstrong units.

Roentgenograms of the skull revealed the osteolytic phase of Paget's disease. An osteolytic process also involved the bodies, pedicles and neural arches of the fifth and sixth cervical vertebrae with an associated compression fracture that forced bone fragments into the spinal canal (Fig. 1, *A* and *B*). The intervertebral spaces were maintained. Although the appearance of the cervical spine was thought to be more compatible with metastatic carcinoma, a diagnosis of Paget's disease was considered in view of the skull findings.

Microscopic examination of a biopsy specimen taken from the fifth cervical vertebra showed a maze of irregular bone trabeculae with large numbers of osteoblasts and osteo-

* From the Department of Radiology, Columbia–Presbyterian Medical Center, New York, New York.
† Assistant Professor of Radiology.
‡ Professor of Radiology, and Chairman of the Department of Radiology.

TABLE I

NEUROLOGIC COMPLICATIONS OF PAGET'S DISEASE IN THE CERVICAL SPINE

Case No. Unit No.	Sex	Age (yr.)	Neurologic Signs and Symptoms	Physical Examination	Roentgen Findings and Compression
I. S.M. 1599036	M	42	1 year loss of power in hands 6 months numbness in fingers, and 4 months numbness in toes	Atrophy of right hypothenar muscles Weakness of extremities Decreased position and vibratory sense. Hyperreflexia, bilateral	Marked destruction of the bodies of C5 and C6 with marked increase in the anteroposterior diameter and compression of C5 and C6. Marked demineralization of the lamina and spinous processes of C5 and C6 (Fig. 1, *A* and *B*) Skull: Osteoporosis circumscripta of the frontal bones
II. J.T. 1538337	M	69	2 years progressive weakness of lower extremities. Chronic difficulty in walking, low back pain 6 months weakness of left upper extremity	Spastic quadriparesis, more marked in lower extremities. Spastic gait. Bilateral hyperactive reflexes and Babinski signs. Atrophy of small hand muscles	C5, C6, C7 and odontoid—amorphous increase of bone density, loss of trabecular detail with decreased heights and increased anteroposterior diameters of bodies; demineralization, increased size of neural arches. Partial destruction of anterior superior body of C5. Osteophytes of C3-C7. Narrowed C5-C6, C6-C7 interspaces (Fig. 2*A*) Skull: Osteoporosis circumscripta of occiput Myelogram: August 10, 1961—partial obstruction of C5-C6 interspace. Large osteophytes of C4-C5, C5-C6; smaller at C3-C4 (Fig. 2*B*)
III. M.M. 109940	M	63	Quadriplegic after fall from ladder	Loss of all sensation and motor power below C4 Nystagmus on right lateral gaze	Posterior subluxation of C4 on C5. Body of C4 demineralized, slight accentuation of cortices. Body of C5—amorphous increase in bone density of posterior superior half of body. Cortex ill defined, dense. Body of C6 and arches of C4, C5 and C6—coarse trabeculae, dense cortices, radiolucent central areas. Body of C4, C5 and C6—increase in the anteroposterior diameters, decreased heights. Narrowed C4-C5, C6-C7 interspaces with osteophytes (Fig. 3)
IV. A.L. 1531210	F	50	Occipital headaches, back and leg pain	Swelling of lower extremities	C6—homogeneous increase in bone density and anteroposterior diameter. Slight decrease in height. Increased density of neural arch and increase of spinous process, with ill defined trabeculae (Fig. 4). Paget's disease (skull, clavicle, dorsolumbar spine, tibiae, pelvis)
V. E.B. 1416443	M	80	Trauma to neck. Since then vertigo, tinnitus, tremor of upper extremities, gait disturbance, numbness in legs	Absent deep tendon reflexes, decreased position sense of both lower extremities	Body of C2 enlarged, dense, with loss of trabecular detail and interspace obliterated. Lamina and spinous process of C2 markedly enlarged with thick cortices, radiolucent centers. C2-C3 zygoapophyseal joint obliterated (Fig. 5)
VI. L.K. 1433462	M	81	Numbness of right half of body for 18 months	Partial right hemianesthesia	All cervical vertebrae involved. Coarse trabeculae, thick cortices, radiolucent centers. Arches and spinous processes involved. Narrowed interspaces and zygoapophyseal joints C3-C4, C4-C5. Thoracolumbar spine and pelvis involved Skull negative
VII. A.M. 245189	M	66	1 year of blurred vision of left eye. Pituitary adenoma	Visual field defect	All cervical vertebrae involved. Coarse trabecular thick cortices. Marked narrowing C3-C4, C4-C5, C5-C6 interspaces, osteophytes Skull not involved

TABLE I-(*continued*)

Case No. Unit No.	Sex	Age (yr.)	Neurologic Signs and Symptoms	Physical Examination	Roentgen Findings and Compression
VIII. B.N. 1097676	M	68	Convulsions since 1952	Diminished left arm swing, unsteady finger-nose test, ?Babinski sign	Entire cervical spine involved—bodies and neural arches. Classic appearance. ?Enlarged anteroposterior diameter—C_3, C_4, and C_5. Narrowed C_5-C6 interspace with osteophytes C_5, C6 and anterior to C_4-C_5 interspace (fragmented). Lumbar spine and pelvis involved Skull not involved Pneumoencephalogram—cortical atrophy
IX. A.P. 1709592	M	68	None	Bowed left leg	Entire cervical spine involved. Classic appearance. Markedly radiolucent, demineralized bodies with slight cortical accentuation. C6-increase of anteroposterior diameter, and decreased height. Entire spine, pelvis, femora, scapulae, clavicles, and ribs involved Skull not examined
X. J.R. 222509	M	81	Known Parkinsonian	Intentional tremor	Entire cervical spine involved. Marked homogeneous increase in bone density, particularly odontoid and posterior elements. Indistinct trabecular pattern. C_5 and C6 bodies decreased in height, increased anteroposterior diameters. Large osteophytes in the anterior inferior margins of C_5 and C6. Narrowed C_5-C6, C6-C7 interspaces Mandible humeri, clavicles involved No skull roentgenograms
XI. J.Y. 227458	M	70	Pain in hands, knees, and ankles	Swelling and redness of hands, ankles and knees	Entire cervical spine involved—bodies and neural arches; classic appearance. Spinous processes not involved, disk spaces preserved. Lumbar spine involved No skull roentgenograms

clasts and highly vascular intervening connective tissues compatible with Paget's disease. There was no evidence of neoplastic disease.

Comment. The osteolytic phase of Paget's disease is most commonly seen in the skull[19] and tibia[14] and is quite rare in the spine. Involvement of the twelfth dorsal and second lumbar vertebrae with associated compression fractures and neurologic symptoms was described in 2 patients by Henze.[5] Although the presence of Paget's disease in the skull should have been a clue to the correct diagnosis, the infrequency of cervi-

TABLE II

NUMBER OF CERVICAL VERTEBRAE INVOLVED

Total Number of Cervical Vertebrae Involved	Total Number of Cases	Case Numbers
1	1	IV
2	2	II and V
3	2	I and III
7	6	VI, VII, VIII, IX, X and XI
	—	
Total	11	

TABLE III

NUMBER OF CASES WITH SKULL INVOLVEMENT

	Total Number of Cases	Case Numbers
Skull involved	4	I, II, IV and V
Skull not involved	3	VI, VII and VIII
No skull roentgenograms available	4	III, IX, X and XI
	—	
Total	11	

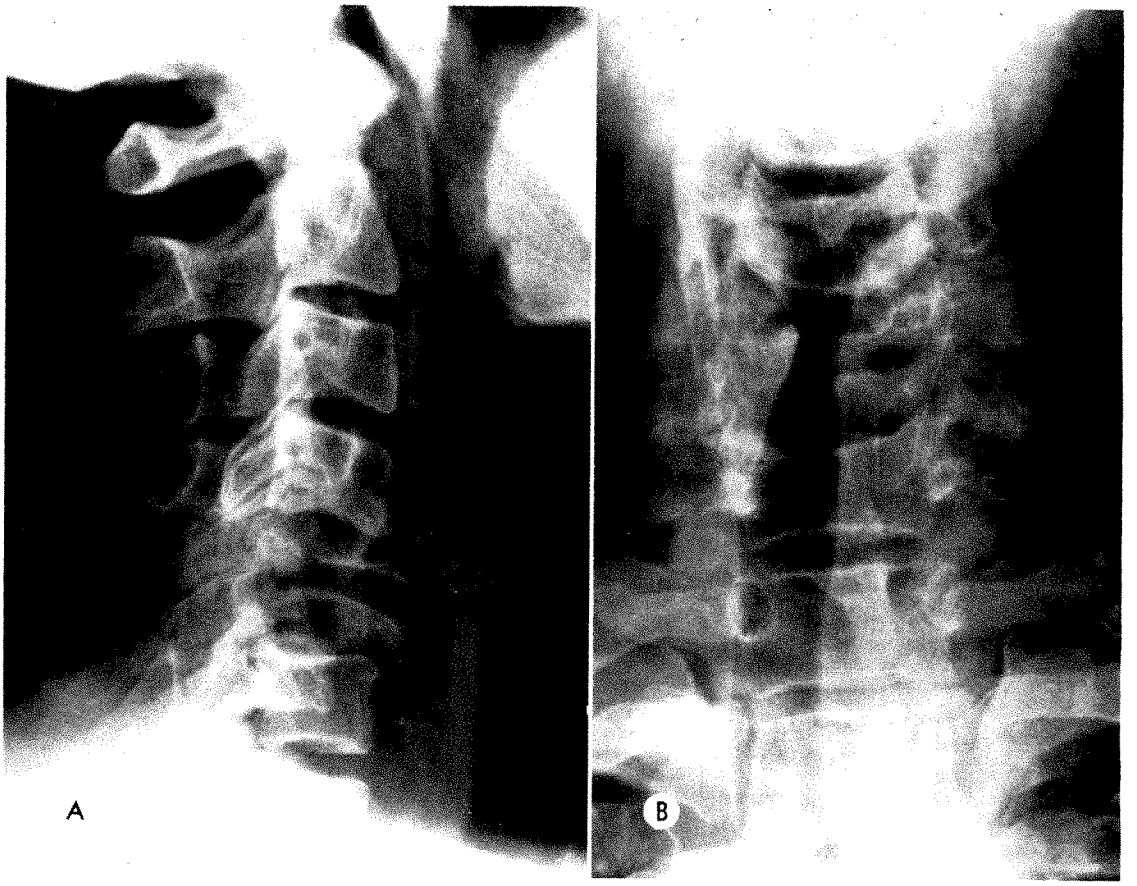


FIG. 1. Case 1. (*A*) Marked destruction and compression of the bodies of C_5 and C6 in a 42 year old male with an enlarged nodular thyroid and numbness and weakness of the upper extremities. Note preservation of the intervertebral spaces. Osteoporosis circumscripta was present in the frontal bone. Vertebral biopsy disclosed Paget's disease. (*B*) Lateral view.

cal spine involvement and the absence of the typical reparative phase of Paget's disease seemed to favor the diagnosis of metastatic disease.

Microscopic examination during the osteolytic phase will reveal only slender bone trabeculae with abundant osteoblasts and vascular connective tissue. The mosaic pattern is a result of the reparative phase.[7]

CASE II. J.T. was a 69 year old male with a 2 year history of progressive weakness of the lower extremities, low back pain and difficulty in walking. Physical examination revealed generalized weakness, atrophy of the small muscles of the hand, and spastic quadriparesis more pronounced in the lower extremities. The serum alkaline phosphatase was 80 King-Armstrong units.

Roentgenograms of the cervical spine showed an amorphous increase in density of the bodies of the fifth, sixth, and seventh cervical vertebrae, with decreased heights and increased anteroposterior dimensions. Osteophytes were present on the anterior margins of the vertebral bodies from C_3 through C_7. The intervertebral disks between C_5 and C6, and C6 and C_7 were narrowed. Coarse trabeculation was present in the posterior aspects of the vertebral bodies of C_5 and C6 as well as the neural arches. Some destruction and fragmentation was noted at the upper, anterior border of C_5 (Fig. 2, *A* and *B*).

Evidence of Paget's disease was present in the pelvis, lumbar and dorsal spine and skull (osteoporosis circumscripta).

Laminectomy and spinal cord decompression were carried out. The left C_5-C6 foramen was almost totally occluded.

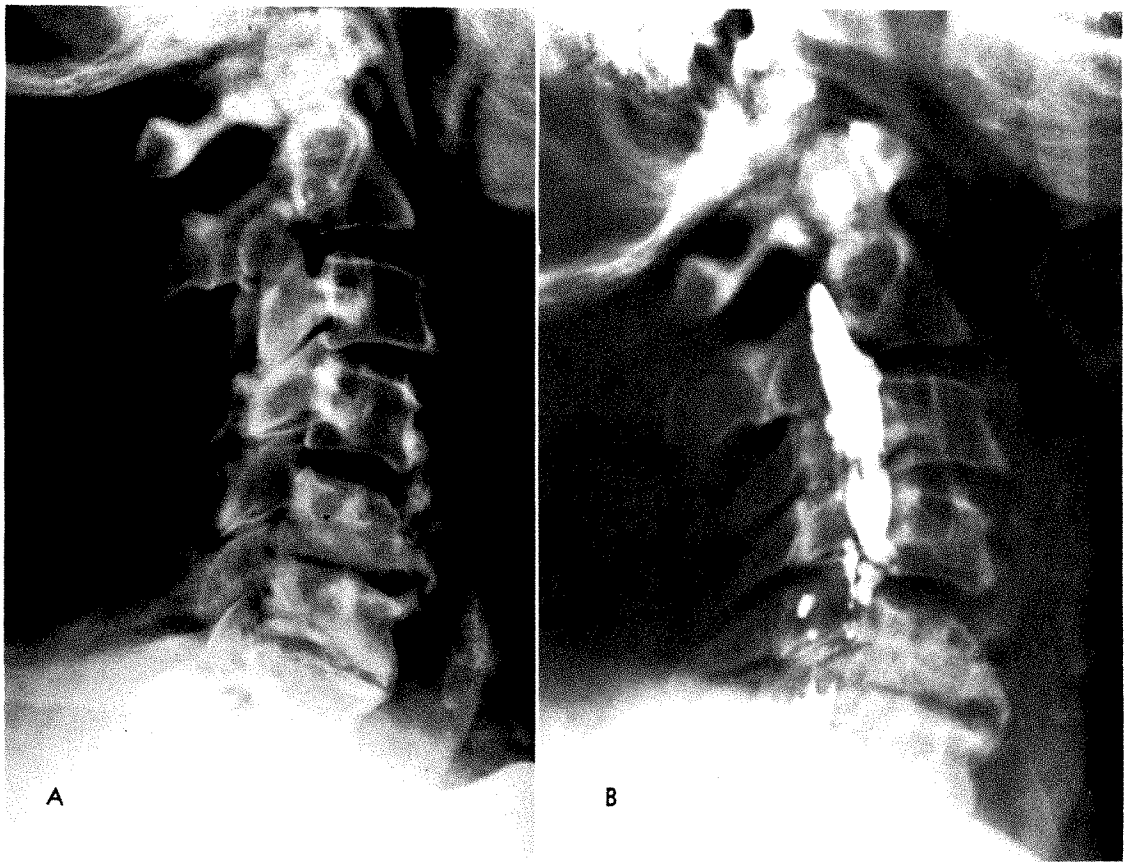


Fig. 2. Case II. (*A*) Paget's disease and degenerative disease in the lower cervical vertebrae of a 69 year old male with spastic quadriparesis. Degenerative changes tend to mask the evidence of Paget's disease best seen in the neural arches and spinous processes. Osteoporosis circumscripta was present in the occipital bone. Paget's disease proven by biopsy of lamina. (*B*) Myelogram shows partial obstruction at the C_5-C6 interspace. Lateral view.

Microscopic examination of excised bone fragments confirmed the diagnosis of Paget's disease.

Comment. The presence of degenerative changes tended to obscure the diagnostic roentgenologic features of Paget's disease, although coarse trabeculae could be seen in some areas. In contrast to Case I, no vertebral collapse had occurred and the neurologic symptoms were the result of bone proliferation.

Schmorl[12] has pointed out that when adjacent vertebrae are affected by Paget's disease, it may involve the intervertebral disk which may be replaced by bone with resultant osseous fusion.

Case III. M.M., a 63 year old white male, became quadriplegic after a fall. Roentgenograms of the cervical spine showed an area of homogeneous sclerosis involving the posterior superior portion of the body of C_5. The body of C_4 was demineralized and there was posterior subluxation of C_4 on C_5. The body of C6 and the arches of C_4, C_5 and C6 showed coarse trabeculae, dense cortices and relatively radiolucent central areas (Fig. 3). Postmortem examination 2 weeks later revealed traumatic myelomalacia of the cervical cord. Microscopic examination of the body of C_5 showed evidence of Paget's disease.

Comment. One may speculate that the underlying Paget's disease may have contributed to the severe neurologic effects of the trauma. Vertebral collapse, dislocation or fracture have been observed spontane-

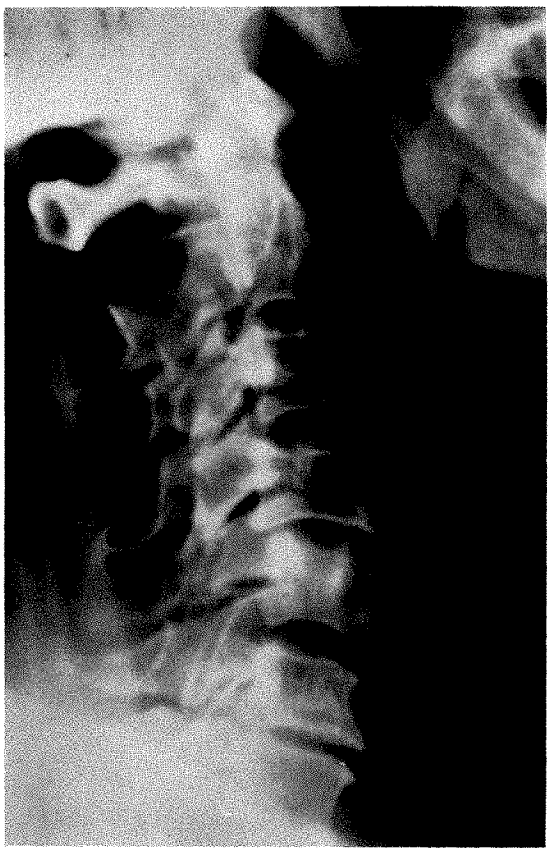


FIG. 3. Case III. A 63 year old white male with autopsy proven Paget's disease of C5. Note involvement of spinous process.

ously or resulting from relatively mild trauma. In the case reported by Whalley,[18] the patient experienced neurologic symptoms while coughing or sneezing.

The absence of coarse trabeculation, bone overgrowth and evidence of Paget's disease elsewhere, makes a correct antemortem diagnosis impossible. Non-neoplastic vertebral sclerosis should be considered as an alternative diagnosis when only a portion of the vertebral body is involved.[1] Paget's disease, however, almost always involves the entire vertebral body.

CASE IV. A.L. was a 50 year old white female with roentgen evidence of Paget's disease involving the skull, clavicles, tibiae, pelvis, thoracic and lumbar spine. She complained of pain in the back, occiput and legs.

Roentgenograms of the cervical spine disclosed a diffuse, homogeneous increased density of the entire body of C6 which was slightly decreased in height and increased in its anteroposterior diameter (Fig. 4). The rest of the cervical spine was normal.

Comment. Despite the absence of histologic verification, the presence of extensive skeletal involvement by Paget's disease, together with a long follow-up (6 years) and the absence of known neoplastic disease makes it most likely that the changes in the sixth cervical vertebra are also due to Paget's disease. Otherwise, the appearance suggests Hodgkin's disease or osteoblastic metastases.

CASE V. E.B. was an 80 year old male, who



FIG. 4. Case IV. A 50 year old female with Paget's disease of skull, clavicle, tibiae, pelvis, thoracic and lumbar spine. The homogeneous osteoblastic response of a single vertebra (C6) suggests metastatic disease. The presence of widespread Paget's disease and the absence of known neoplastic disease make Paget's disease a more likely diagnosis.



Fig. 5. Case v. Paget's disease of the entire axis in an 80 year old male with absent deep tendon reflexes and decreased position sense in lower extremities. Note encroachment on the spinal canal by the enlarged odontoid.

had complained of vertigo, tinnitus, gait disturbance and numbness of the legs since an episode of head trauma 2 years before. Examination revealed absent deep tendon reflexes and decreased position sense in both lower extremities. The sensory examination was normal.

Roentgen examination of the skull revealed typical Pagetoid changes involving the entire second cervical vertebra including the odontoid process (Fig. 5). The lamina and spinous processes of C2 were markedly enlarged with thick cortices and radiolucent centers. The first and third cervical vertebrae were not involved and the rest of the cervical spine was not visualized.

Comment. Involvement of the axis by Paget's disease is extremely rare and only two other examples have been reported.[10,18] In the patient described by Whalley,[18] the axis, atlas and skull were involved and the spinal canal was narrowed by the enlarged odontoid. There was also atlanto-occipital dislocation and paraplegia. In the patient reported by Ramamurthi and Visvanathan,[10] the axis alone was involved and the spinal cord was compressed between the enlarged odontoid and the neural arch of the atlas causing paraplegia.

DISCUSSION

The typical roentgenographic appearance of fully developed Paget's disease is easily recognized, but in the cervical spine it occasionally may be simulated or obscured by degenerative changes. The osteolytic phase occurs in the skull and tibia. Because of its rarity in the cervical spine and its frequent association with vertebral collapse, it may be confused with metastatic disease. It may also be mistaken for a vertebral hemangioma because of the presence of thick vertical trabeculae.[15] Involvement of the neural arch, spinous process and transverse processes, areas not usually affected by hemangioma, greatly favors the diagnosis of Paget's disease. In 9 of our 11 patients, the neural arch was involved.

The appearance of metastatic disease is also simulated by Paget's disease when the vertebral body is homogeneously dense without evidence of enlargement.

The nervous system may, therefore, be affected by Paget's disease in three ways:

1. Reduction in the lumens of the intervertebral foramina and spinal canal by gradual overgrowth of the vertebral bodies and neural arches.
2. Vertebral collapse, dislocation or fracture. When this occurs the onset of symptoms may be sudden.
3. Interference with the blood supply of the spinal cord due to compression by bone overgrowth or vertebral collapse.

Wyllie,[20] in 1923, was the first to point out the neurologic complications of Paget's disease when he described 2 patients with compression of the thoracic spinal cord.

In 1937, Garcin *et al.*[3] were the first to describe compression of the cervical cord. Of the previously reported 29 cases of Paget's disease of the cervical spine, cord compression occurred in 7. If the present series is included, the incidence of spinal cord involvement is 28 per cent (11 of 40 cases).

SUMMARY

1. Eleven cases of involvement of the cervical spine by Paget's disease are reported.

2. Three patients had evidence of spinal

cord compression confirmed by operative or autopsy findings while a fourth is experiencing symptoms probably resulting from subluxation and mild compression.

3. The roentgenographic appearance may closely simulate osteolytic or osteoblastic carcinoma and may be difficult to recognize as Paget's disease. Involvement of the neural arch, particularly when accompanied by involvement of the spinous process, points strongly toward Paget's disease, since it was present in 9 of the 11 cases.

Frieda Feldman, M.D.
Department of Radiology
Columbia–Presbyterian Medical Center
622 West 168th Street
New York, New York 10032

REFERENCES

1. ACKERMANN, W., and SCHWARZ, G. S. Non-neoplastic sclerosis in vertebral bodies. *Cancer*, 1958, *11*, 703–708.
2. DICKSON, D. D., CAMP, J. D., and GHORMLEY, R. K. Osteitis deformans: Paget's disease of bone. *Radiology*, 1945, *44*, 449–470.
3. GARCIN, R., VARAY, A., and DIMO, H. Effondrement vertébral aïgu au cours d'une maladie osseuse de Paget. Quadriplégie transitoire. Syndrome de Brown-Séquard résiduel: contribution à l'étude des complications médullaires de la maladie de Paget. *Rev. neurol.*, 1937, *67*, 761–789.
4. GUTMAN, A. B., and KASABACH, H. Paget's disease (osteitis deformans): analysis of 116 cases. *Am. J. M. Sc.*, 1936, *191*, 361–380.
5. HENZE, H. Osteitis deformans (Paget) of spine. *Radiologie*, 1964, *4*, 6–9.
6. HILLMAN, R. W. Compression of spinal cord in Paget's disease. *Brooklyn Hosp. J.*, 1941, *3*, 155–162.
7. JAFFE, H. L. Paget's disease of bone. *Arch. Path.*, 1933, *15*, 83–131.
8. JANETOS, G. P. Paget's disease in cervical spine. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1966, *97*, 655–657.
9. MOORE, S. Osteitis deformans: theory of its etiology. *J. Bone & Joint Surg.*, 1951, *33A*, 421–430.
10. RAMAMURTHI, B., and VISVANATHAN, G. S. Paget's disease of axis causing quadriplegia. *J. Neurosurg.*, 1957, *14*, 580–583.
11. ROSENKRANTZ, J. A., WOLF, J., and KAICHER, J. J. Paget's disease (osteitis deformans). *Arch. Int. Med.*, 1952, *90*, 610–633.
12. SCHMORL, G. Über Ostitis Deformans Paget. *Virchows Arch. f. path. Anat.*, 1932, *283*, 694–751.
13. SCHWARZ, G., and REBACK, S. Compression of spinal cord in osteitis deformans (Paget's disease) of vertebrae. AM. J. ROENTGENOL. & RAD. THERAPY, 1939, *42*, 345–366.
14. SEAMAN, W. B. Roentgen appearance of early Paget's disease. AM. J. ROENTGENOL. & RAD. THERAPY, 1951, *66*, 587–594.
15. STEINBACH, H. L. Some roentgen features of Paget's disease. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1961, *86*, 950–963.
16. TENG, P., GROSS, S. W., and NEWMAN, C. M. Compression of spinal cord by osteitis deformans (Paget's disease), giant-cell tumor and polyostotic fibrous dysplasia (Albright's syndrome) of vertebrae: report of 4 cases. *J. Neurosurg.*, 1951, *8*, 482–493.
17. TURNER, J. W. A. Spinal complications of Paget's disease (osteitis deformans). *Brain*, 1940, *63*, 321–349.
18. WHALLEY, N. Paget's disease of atlas and axis. *J. Neurol., Neurosurg. & Psychiat.*, 1946, *9*, 84–86.
19. WILNER, D., and SHERMAN, R. S. Roentgen diagnosis of Paget's disease (osteitis deformans). *M. Radiog. & Photog.*, 1966, *42*, 35–78.
20. WYLLIE, W. G. Occurrence in osteitis deformans of lesions of central nervous system. *Brain*, 1923, *46*, 336–351.

Vol. 105, No. 2

SPONTANEOUS EPIDURAL SPINAL HEMORRHAGE

By MARTIN E. HARRIS, M.D.*
ALBUQUERQUE, NEW MEXICO

EPIDURAL spinal hemorrhage is a rare entity. Known causes include trauma,[9] anticoagulant therapy,[2] hemophilia[8] and vascular anomalies.[3] The idiopathic form, spontaneous nontraumatic epidural hematoma, is extremely rare having been reported only 50 times since its initial description by Jackson in 1869.[5] It is the purpose of this paper to present such a case.

REPORT OF A CASE

A 66 year old white male physician presented with a history of long standing arthritic involvement of the back. The pain had been intermittent, but for several months prior to admission he had developed pain radiating into his left leg, starting in the fleshy part of the buttock and spreading down to the popliteal region. The pain was not aggravated by coughing, sneezing, straining or bending, but he had noticed that the pain was less severe in the recumbent position. For a few months he had also noticed numbness on the lateral aspect of the left heel, but this had subsequently disappeared. Approximately 1½ months prior to admission he had a period of a few days during which the pain was completely gone, but it recurred and during the month prior to admission the pain became progressively worse. The past history was unremarkable. There was no history of trauma, hypertension, diabetes, tuberculosis, or ingestion of drugs.

Neurologic examination revealed a normal upright posture. Forward flexion to about 45° produced pain in the left buttock spreading into the left sciatic region. The head-dropping and jackknife tests were negative. In the recumbent position straight leg raising was limited to about 30° on the left with positive Lasègue and popliteal pressure tests. On the right there was no limitation of movement and these tests were negative. Sensation was diminished to both touch and pain over S_1 on the left. Deep tendon reflexes showed complete absence of the left patellar and left Achilles reflexes. The lumbar spine showed mild tenderness at the lumbosacral interspace but there was no paravertebral tenderness.

Blood cell count and urine analysis were normal. The cerebrospinal fluid contained 1 lymphocyte and 2 white blood cells/cm.^{3}; proteins were 53.5 mg. per cent and sugar, 63 mg. per cent.

Roentgenographically, the lumbosacral spine showed diffuse arthritic changes with anterior bridging as well as lateral hypertrophy around the joints. The sacroiliac and hip joints were normal. Myelography revealed a large, left lateral extradural filling defect at the level of the lumbosacral interspace (Fig. 1, *A*, *B* and *C*). It interfered considerably with the flow of pantopaque which was displaced around it to the right. The caudal sac inferiorly was unremarkable and the remainder of the lumbar subarachnoid space was normal. The opaque medium was gravitated to the level of D_{12}. Due to the patient's great discomfort, no attempt was made to visualize the dorsal region.

The diagnostic impression was that of a large extradural defect on the left side of L_5-S_1, consistent with a large, left lateral disk herniation. A laminectomy was performed at L_5-S_1. At surgery there was difficulty in removing the ligamentum flavum because of arthritic overgrowth and adhesions. There was evidence of old hemorrhage and a "granular" tissue attached to the surface of the dura. The disk space was visualized, but the disk was not herniated or extruded. The disk capsule was opened and the disk removed. However, it was not felt that this was the cause of the patient's pain, nor did it produce the defect seen on the myelogram. As the investigation was carried further cephalad, it was noted that the epidural space was filled with a granular material which was attached to the dura. At one point, the dura was inadvertently opened permitting spinal fluid to escape. No herniation of disk material could be found in the epidural space. The granular tissue was removed and hemostasis secured. The patient tolerated the

* Associate Radiologist, Presbyterian Hospital Center; Clinical Associate, Department of Radiology, University of New Mexico, College of Medicine, Albuquerque, New Mexico.

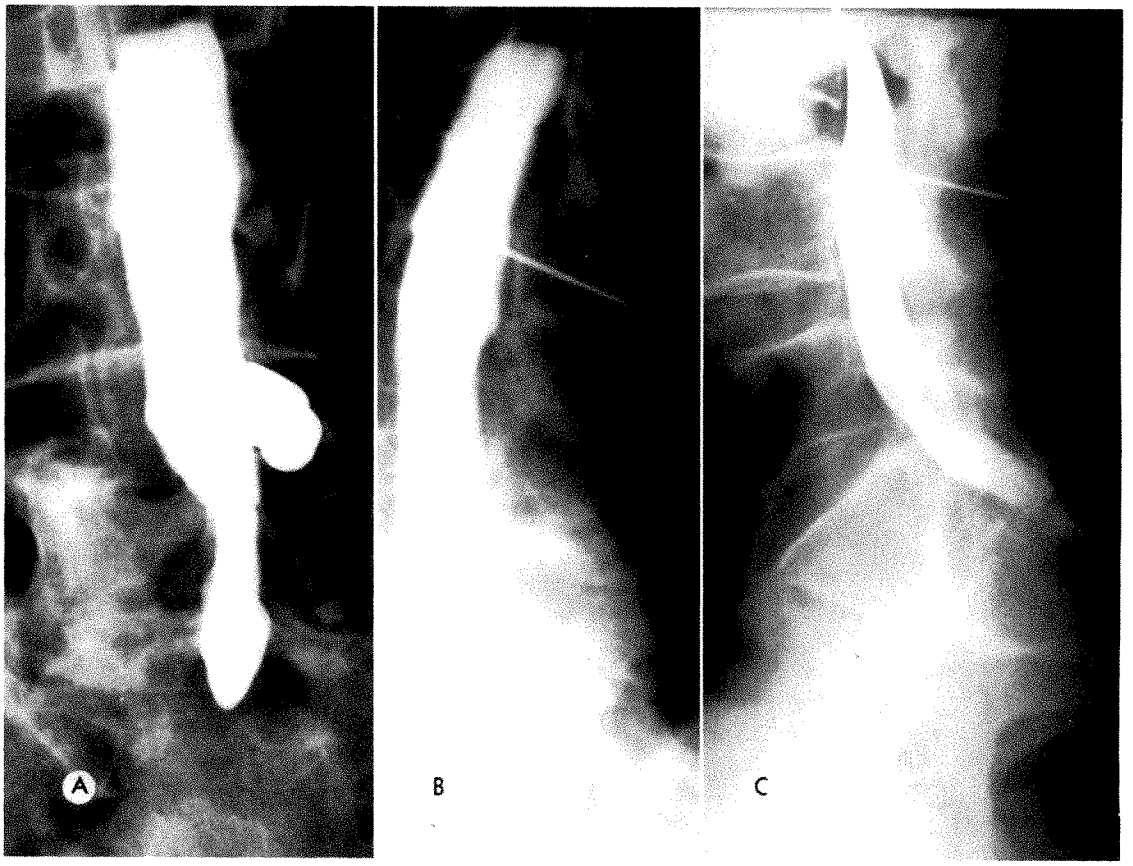


FIG. 1. (*A*) Anteroposterior spot roentgenogram showing a large, left lateral extradural defect at the L_5-S_1 interspace. (*B*) Left oblique spot roentgenogram showing posterolateral extent of defect. (*C*) Lateral roentgenogram showing relatively minor abnormality.

procedure well. The postoperative course was uneventful and the patient made a full recovery.

The pathology examination revealed "portions of fibrocollagenous tissue with focal necrosis and old and recent hemorrhage."

DISCUSSION

The syndrome of spontaneous epidural hemorrhage is uncommon, usually causing acute compression of the spinal cord or cauda equina.[6] It occurs slightly more frequently in males than females. The age incidence is from 1½ years to 79 years with the greatest frequency in the 51-60 year age group. The main symptoms are pain in the spinal region, motor weakness, numbness, and urinary retention. Severe pain is initially localized at the affected spinal level, but later becomes more extensive. Radicular pain soon follows along the distribution of the affected nerve roots.

The onset of pain is related to an insignificant strain such as micturition, defecation, bending forward, turning in bed, lifting small weights, or during sleep. Motor weakness usually progresses rapidly and the patient soon becomes prostrate. In most cases paresis is found within 3 hours. Flaccid motor weakness and diminished tendon reflexes occur more often than spasticity and hyperreflexia. Numbness is usual and clearly defined sensory levels corresponding to the cord lesion are clearly definable. Urinary retention occurs in the majority of the patients. The symptoms may, however, simulate those of an herniated disk as they did in this case and one other reported case.[11] Both these cases

occurred in the lumbar area—the explanation for their more chronic course may be due in part to the greater volume of space allotted to the spinal contents in the lumbar area. If the hemorrhage occurs slowly, the spinal nerves and cauda equina may have sufficient time and space to partially accommodate the pressure created by the hematoma.

The cerebrospinal fluid protein levels are usually over 45 mg. per cent, ranging from 22 mg. per cent to 2,800 mg. per cent. Manometric tests show complete or partial block in 75 per cent of cases. Roentgenograms of the spine are normal, but myelography has been positive in 30 of 33 patients studied. The various myelographic abnormalities reported include complete block, streaking of the pantopaque column, an extradural defect or an intramedullary defect. The lesion may be seen at any spinal level, but is most frequently encountered in the thoracic area.[10]

Therapy consisted of laminectomy in 43 patients. Ten of these patients were dead in 5 months. Of the remaining 33 who survived, 17 were restored to normal or greatly improved. A moderate permanent disability occurred in 9 cases and in 6 there was no improvement. All 8 patients, in whom no surgical treatment was attempted died within 9 days.

SUMMARY

A case of spontaneous epidural hematoma is described and the clinical and roentgenographic findings are discussed.

It is emphasized that spontaneous epidural hematoma with spinal cord compression is a distinct clinical entity which should be considered in the differential diagnosis of acute spinal cord syndromes or acute ruptured intervertebral disk disease.

Department of Radiology
Presbyterian Hospital Center
Albuquerque, New Mexico 87106

REFERENCES

1. Ainslie, J. P. Paraplegia due to spontaneous extradural hemorrhage. *Brit. J. Surg.*, 1958, *45*, 565–567.
2. Alderman, D. B. Extradural spinal-cord hematomas: report of case due to dicumarol and review of literature. *New England J. Med.*, 1956, *255*, 839–842.
3. Brion, S., Netsky, M G, and Zimmerman, H. M. Vascular malformations of spinal cord. *A.M.A. Arch. Neurol. & Psychiat.*, 1952, *68*, 339–361.
4. Cooper, D. W. Spontaneous epidural hematoma: case report. *J. Neurosurg.*, 1967, *26*, 343–344.
5. Jackson, R. Case of spinal apoplexy. *Lancet*, 1869, *2*, 5.
6. Kaplan, L. I., and Denker, P. G. Acute nontraumatic spinal epidural hemorrhage *Am. J. Surg.*, 1949, *78*, 356–361.
7. Markham, L., I, and Stahlman. Syndrome of spontaneous spinal epidural hematoma: report of three cases. *J. Neurosurg.*, 1967, *26*, 334–342.
8. Priest, W. M. Epidural haemorrhage due to haemophilia causing compression of spinal cord. *Lancet*, 1935, *2*, 1289–1291.
9. Schultz, E. C., Johnson, A. C., Brown, C. A., and Mosberg, W. N. Paraplegia caused by spontaneous spinal epidural hemorrhage. *F. Neurosurg.*, 1953, *10*, 608–616.
10. Shapiro, R. Myelography. Year Book Medical Publishers, Chicago, 1962.
11. Svien, H. J., Adson, A. W., and Dodge, H. W., Jr. Lumbar extradural hematoma: report of case simulating protruded disk syndrome. *J. Neurosurg.*, 1950, *7*, 587–588.

INTRASPINAL DERMOIDS AND EPIDERMOIDS

By S. K. GUPTA, M.D., D.M.R.,* *and* Y. P. BHANDARI, M.D., D.M.R.E.†
PONDICHERRY, INDIA

DERMOIDS and epidermoids of the central nervous system are uncommon lesions. According to Fleming *et al.*[6] they represent less than 1 per cent of all tumors within the skull, and in the spinal canal they are even less frequently encountered. Cruveilhier[4] first introduced the term "tumor perlée" in 1829 when he reported 2 cases. After that, embryonic tumors of the spinal canal have been reported by various authors, a few among them giving comprehensive reviews.[1,2,7,9,11] Up to 1949, Sachs and Horrax[16] could find only 59 cases of spinal dermoids and epidermoids in the literature and they added 2 cases of their own. Since then, additional cases were reported by Moore and Walker[13] (1 case), Manno *et al.* [12] (1 case), Sloof, Kernohan and MacCarty (4 cases), and very recently by Roth *et al.*[15] (1 case).

Because of the rarity of these tumors we report 2 additional cases.

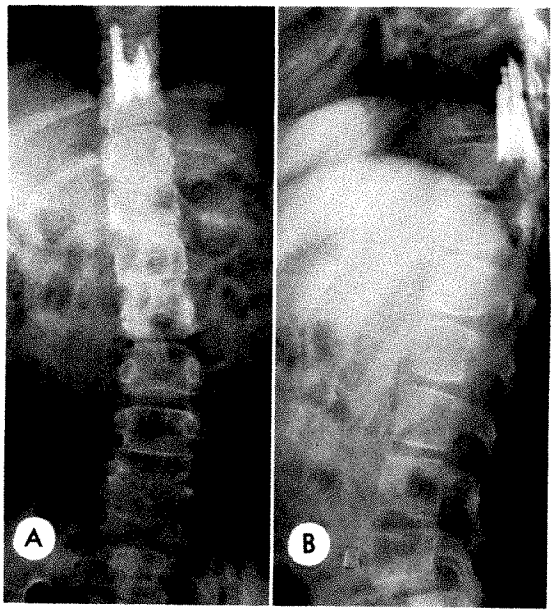


FIG. 1. Myelography done via the cisternal route in a case of intraspinal epidermoid. (*A*) Anteroposterior view (*B*) lateral view. A complete block is seen to the contrast column at the level of D10 vertebra. The vertebral canal shows widening from the lower part of D10 to L2. The posterior aspects of the vertebrae demonstrate arcuate indentation, the pedicles show flattening and there is an increase in the interpedicular distance.

REPORT OF CASES

CASE 1. D.S. a 14 year old male was admitted to the medical ward of V.J. Hospital/Medical College, Amritsar. His illness started 5 years prior to admission with loss of control of the bladder function. He also had deformity and an ulcer of the right foot. Two years later he developed low back pain.

On examination the right foot showed equina varus deformity and there was a painless ulcer on its lateral aspect. The right lower limb showed moderate wasting and loss of power. The sensations were dulled on the anterolateral surface of the right lower limb and the lateral part of the dorsum of the right foot. The plantar reflex on the right side was indeterminate. No neurologic abnormality was found in the left lower limb. The spine in the lumbar region showed tenderness and scoliosis to the left. The movements of the spine were also limited. Cerebrospinal fluid examination revealed increased globulins and total proteins (720 mg./100 ml.).

Plain roentgenographic study of the spine showed widening of the spinal canal from the lower part of D10 to L2 vertebra, both in the anteroposterior and lateral diameters (Fig. 1, *A* and *B*). The pedicles showed erosions and there was increase in the interpedicular distance. The posterior aspects of the bodies of the vertebrae showed minimal arcuate indentations.

Myelography was performed via the cisternal route. Complete block was present at the level of the 10th dorsal vertebra (Fig. 1, *A* and *B*).

A diagnosis of intraspinal tumor was made and the patient transferred to the Orthopedic section for operative removal of the tumor.

* Assistant Radiologist, V. J. Hospital/Medical College, Amritsar (Pb.). At present, Lecturer in Radiology, JIPMER, Pondicherry, India.
† Assistant Radiologist, V.J. Hospital/Medical College, Amritsar, India.

At exploration, on incising the dura, thick creamy material escaped with firm shiny flakes covered by a membrane resembling a cyst. The underlying spinal cord appeared normal. The pathologic diagnosis was epidermoid cyst.

Case II. A.K. a 16 year old male was admitted to the orthopedic ward of V.J. Hospital/Medical College, Amritsar, with paraplegia. The patient had 2 bony hard swellings of the back in the lower thoracic region since birth. At the time he started walking, a weakness of the left lower limb was noticed. He used to walk with a limp. The weakness gradually increased and he became more and more disabled. A year prior to admission he also developed progressive weakness of the right lower limb. For the last 6 months the patient was almost bedridden. He had lost control of his vesical and rectal sphincters. He occasionally had episodes of spontaneous spasm and clonus in which the limb got straightened and cross legged, with adduction at the hips and extension of the knees. He preferred to sit cross legged, because in this position he experienced no spasm.

Examination revealed scoliosis of the dorsal spine to the left and 2 bony hard prominences over the dorsal spine. A few hairs and 2 dimples were also present, one on the top prominence and the other to the left of it. Both lower limbs were equal in length, but the tonus was increased. The power was lost in all groups of muscles except the extensor hallucis longus and the extensor digitorum longus. Complete loss of sensation was present below the inguinal region anteriorly and below the upper gluteal region posteriorly. The tendon reflexes were exaggerated. The Babinski sign was upgoing with a cremasteric reflex. The cerebrospinal fluid showed increased globulins and total proteins (180 mg./100 ml.).

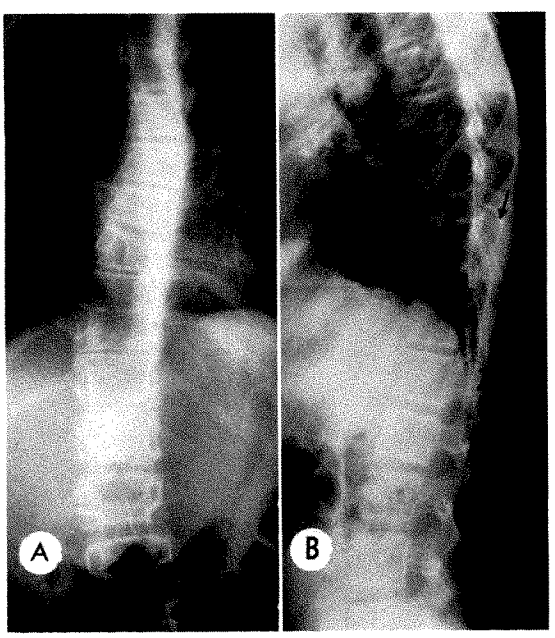


Fig. 2. Plain (*A*) anteroposterior and (*B*) lateral roentgenograms of a case of intraspinal dermoid. Scoliosis of dorsal spine is seen to the left. The pedicles of D9–D12 on the left side show flattening and the vertebral canal shows widening with increase in the interpedicular distance. The spinous processes in this region are not seen. The arrows point to the location of bony prominences.

Plain roentgenograms of the spine showed mild scoliosis to the left, widening of the vertebral canal, flattening of the pedicles, increase in the interpedicular distances and 2 bony prominences (Fig. 2, *A* and *B*). The bone changes extended from D9 to D12. The spinous processes in this region were not seen. In view of the symptoms referrable to his lesion since early childhood and the presence of dimples and hairs on the back, a diagnosis of embryonic intraspinal lesion (dermoid or epidermoid) was made. Myelography was thought superfluous.

An operation was performed, using a midline incision about 6 inches long, elliptical in its lower part, and enclosing the skin over the distal bony prominence. A broad continuous sheet of bone extending between the 2 bony prominences was found (Fig. 3). The thickness of the sheet was that of a normal lamina. A 1 inch broad central portion of the sheet was removed in its entire length along with the lower bony prominence. The upper bony prominence was also partially excised. The ligamentum flavum lying under the sheet was very much thickened. It was removed and the dura was exposed. The upper part of the exposed dura was very tense. The dura was then incised and the spinal cord exposed. The spinal cord was quite large and it was creamy white in color. On longitudinal incision through the cord, whitish creamy material escaped. This was thoroughly removed together with some shreds of semisolid tissue containing a few hairs. The diagnosis of intramedullary dermoid was confirmed.

DISCUSSION

Intraspinal dermoids and epidermoids are clinically an important group of intraspinal tumors, inasmuch as they

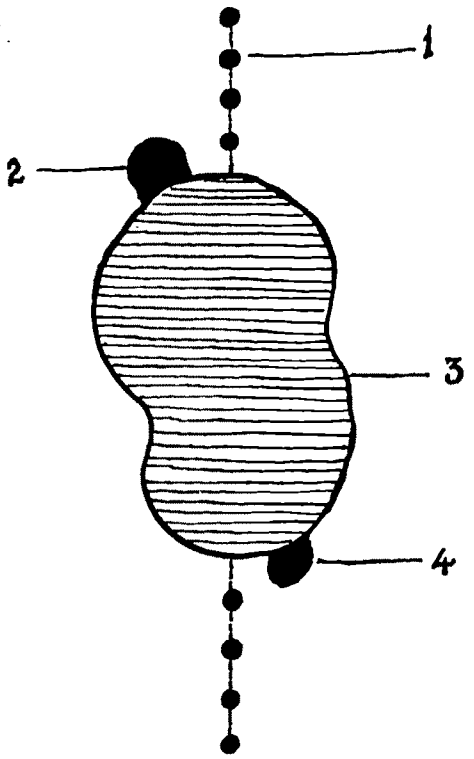


FIG. 3. Schematic diagram of the bony prominences and the sheet seen in the case of intraspinal dermoid (Case 1). 1. Normal spinous processes. 2. Upper bony prominence. 3. Bony sheet. 4. Lower bony prominence.

produce symptoms of spinal cord or root compression like any other intraspinal space occupying lesion. They are composed of elements of skin and are dysembryonic malformations rather than true neoplasms.[5] They arise wherever two ectodermal surfaces fuse in the developing embryo and when an ectodermal implant is retained deep in the surface. This occurs at the 4th week of intrauterine life when the neural ectoderm separates from the cutaneous ectoderm along the mid dorsal aspect of the embryo.[6] As a result of such an inclusion an epidermoid or dermoid may develop between the skin and brain ventricles or the central canal of the spinal cord. A congenital dermal sinus of varying length and completeness may persist in association with these tumors.

Spinal dermoids and epidermoids usually cause gradually progressive symptoms of spinal cord or root compression for many years before a diagnosis is established.[10] The symptoms frequently date back to early childhood and by the time the diagnosis is made, most of these cases are already hopelessly disabled.[14] In our Case II, the symptoms were likewise present from early childhood and he was completely paraplegic and bedridden when the diagnosis was made at the age of 16 years. In Case 1 the symptoms were present for 5 years. The presence of cutaneous dimples and hairs in the middle of back suggests embryonic intraspinal neoplasm.[5] Our Case II showed hairs and cutaneous dimples on the back and in addition had 2 bony prominences in the midline at the site of the intraspinal lesion. These bony prominences along with a sheet of bone extending between them (Fig. 3) are presumably due to mesodermal dysplasia affecting the spinous processes and laminae. Such an association of dermoids and epidermoids (due to neuro-ectodermal dysplasia) and mesodermal dysplasia affecting the spinous processes and laminae does not appear to have been reported in the available literature. Usual skeletal defects found in association with dermoids and epidermoids are spina bifida and hemivertebrae.[1,8]

Dermoids and epidermoids occur more frequently in males; both our cases were males.

According to Epstein[5] dermoids have an affinity for the lumbosacral portion of the spinal canal and are never encountered in the cervical region. Epidermoids, however, occur in a fairly uniform distribution over the thoracic and lumbosacral portion of spinal canal.[16] In one of our cases the epidermoid was located in the dorsolumbar region. In the other the dermoid was found in the lower dorsal region.

Epidermoids and dermoids of spinal canal may have intramedullary or extramedullary intradural or even extradural location. With dermoids, extramedullary intradural location is more frequent than intramedullary location. Craig[3] has stated

that only 2 cases of intramedullary dermoids have been reported. Recently Roth *et al.*[15] reported another case. The epidermoids are almost equally divided between those with intramedullary and those with extramedullary intradural locations. We had one case with intramedullary location and the other with extramedullary intradural location.

Bone changes in the form of widening of the vertebral canal, flattening of the pedicles and arcuate indentation of the dorsal aspect of the bodies of the vertebrae are important findings on plain roentgenography. These changes were present in both of our cases. According to Hannan and Geist[10] 50 per cent of the cases of intraspinal dermoids and epidermoids show bone changes and when present are sufficient for suspecting a diagnosis of intraspinal dermoid or epidermoid. Calcific deposits in the vertebral canal are usually absent; however, massive calcific deposits were seen in the vertebral canal in the case reported by Moore and Walker.[13]

When the plain roentgenograms of the spine are normal, myelographic examination should be employed. Myelography shows a block and there are usually no other characteristic features.

SUMMARY

The roentgenographic and clinical features of one case of intraspinal epidermoid and another of intramedullary dermoid are described.

The importance of a consideration of these lesions in the diagnosis of long standing cases of spinal cord involvement showing bone changes on plain roentgenograms is emphasized.

The case of dermoid (Case II) showed an unusual feature of 2 bony prominences and a bony sheet replacing the spinous processes and laminae in the region of intraspinal lesion.

Associated mesodermal dysplasia is suggested as an explanation for this new bone abnormality observed.

S. K. Gupta, M.D.
Jawaharlal Institute of Postgraduate Medical Education and Research
Pondicherry-6, India

REFERENCES

1. Boldrey, E. B., and Elvidge, A. R. Dermoid cysts of vertebral canal. *Ann. Surg.*, 1939, *110*, 273–284.
2. Bradford, R. K. Intramedullary dermoid cyst. *Ann. Surg.*, 1938, *107*, 107–115.
3. Craig, R. L. Case of epidermoid tumor of spinal cord: review of literature of spinal epidermoids and dermoids. *Surgery*, 1943, *13*, 354–367.
4. Cruveilhier, J. Anatomie Pathologique. Volume II. J. B. Baillière et fils, Publisher, Paris, 1829. Quoted by E. B. Boldrey and A. R. Elvidge.[1]
5. Epstein, B. S. The Spine: A Radiologic Text and Atlas. Lea & Febiger, Philadelphia, 1955.
6. Fleming, J. F. Ross, and Botterell, E. H. Cranial dermoids and epidermoids. *Surg., Gynec. & Obst.*, 1959, *109*, 403–411.
7. Fraser, J. Cystic dermoid tumour of spinal cord. *Surg., Gynec. & Obst.*, 1930, *51*, 162–168.
8. French, L. A., and Peyton, W. T. Mixed tumors of spinal cord. *Arch. Neurol. & Psychiat.*, 1942, *47*, 737–751.
9. Gross, S. W. Concerning intraspinal dermoids and epidermoids, with report of case. *J. Nerv. & Ment. Dis.*, 1934, *80*, 274–284.
10. Hannan, J. R., and Geist, R. M., Jr. Teratomatous tumors of spinal canal: report of two cases. Am. J. Roentgenol. & Rad. Therapy, 1950, *63*, 875–880.
11. List, C. F. Intraspinal epidermoids, dermoids and dermal sinuses. *Surg., Gynec. & Obst.*, 1941, *73*, 525–538.
12. Manno, N. J., Uihlein, A., and Kernohan, J. W. Intraspinal epidermoids. *J. Neurosurg.*, 1962, *19*, 754–765.
13. Moore, W. W., and Walker, E. Intraspinal epidermoid tumor: case report and discussion. *J. Neurosurg.*, 1951, *8*, 343–347.
14. Naffziger, H. C., and Jones, O. W., Jr. Dermoid tumors of spinal cord: report of four cases with observations on clinical test for differentiation of source of radicular pains. *Arch. Neurol. & Psychiat.*, 1935, *33*, 941–958.
15. Roth, M., Hanák, L., and Schröder, R. Intramedullary dermoid. *J. Neurol., Neurosurg. & Psychiat.*, 1966, *29*, 262–264.
16. Sachs, E., Jr., and Horrax, G. Cervical and lumbar pilonidal sinus communicating with intraspinal dermoids: report of two cases and review of literature. *J. Neurosurg.*, 1949, *6*, 97–112.

THE OCCULT INTRASACRAL MENINGOCELE

By IRVING S. YOUNG, M.D.,* *and* ANDRÉ J. BRUWER, M.D.†
SALT LAKE CITY, UTAH, AND TUCSON, ARIZONA

ALTHOUGH, by definition, a meningocele implies a hernial protrusion of the meninges through a defect in the skull or the vertebral column, we shall, for lack of a better term and in order not to confuse the sparse literature on the subject, accept the term "occult intrasacral meningocele," originally used by Enderle.[5]

Occult intrasacral meningoceles are quite rare, as evidenced by the paucity of cases reported in the literature. The purpose of this paper is to describe the entity, present a case, briefly review the literature and discuss possible etiologies.

Intrasacral meningocele (occult meningocele of the sacrum) may be described as an abnormal dilatation of the meninges lying within the confines of the sacral spinal canal. Often the sacral canal is markedly dilated in both sagittal and coronal planes with only a thin shell of bone remaining on the anterior and posterior walls. There may be an associated spina bifida occulta, but to be included in the definition there can be little or no herniation of the spinal membranes. Usually the meningocele cavity communicates with the subarachnoid cul-de-sac by a narrow channel. The meningocele cavity may show evidence of loculation by septa, or separate isolated cavities (multicystic) can exist. Sacral nerves are found to be incorporated in the wall of the cavity or lie just outside, pressed against the bony wall. Two cases have been reported in which the spinal cord extended down into the sacrum (no cauda equina). Intrasacral meningocele should be differentiated from sacral perineural cyst[1] which, as its name suggests, completely surrounds an individual nerve.

Other forms, such as the meningeal cyst or spinal extradural cyst and diverticula of the meninges are not so clearly differentiated. Heppner and Diemath[7] presented a case and reviewed others in which the defects consisted of cysts and diverticula within the epidural space, some connected with the dorsal dura via a fluid-patent channel or thin strand of tissue, and others apparently completely isolated from the meninges. They raised the question of whether these lesions should be considered meningoceles. When located in the sacrum, which can occur, the problem may be one of semantics only. There is one definite difference, however. The great majority of occult intrasacral meningoceles reviewed in this paper involved dilatation of the bony sacral canal; the cysts and diverticula of Heppner and Diemath's report did not.[7]

REPORT OF A CASE

History. A 31 year old white female was admitted to a local hospital for urologic work-up. A few days prior to this admission she had experienced one of her frequent urinary tract infections accompanied by chills, fever, and left-sided flank pain. Neither dysuria nor incontinence was ever prominent among the symptoms, but voiding always required considerable straining and had progressed to complete retention on numerous occasions when infection intervened. She related that even as a child she had had trouble voiding at what she considered a "normal rate," although urinary tract infections were not a problem until the age of 21 years. Previously, treatment had consisted of urethral dilatation or catheterization and the administration of several types of antibiotics.

Physical Examination. Physical examination revealed a sacral scar where she had been operated upon for a pilonidal sinus (details were not available, but she mentioned that prior to this surgery there had been a "lump" under the skin over the sacrum). The other findings were a slight reduction of the left ankle jerk and hyperalgesia in the saddle area.

During this admission a cystometrographic

* Salt Lake City, Utah.
† Tucson Medical Center, Tucson, Arizona.

study was performed and a diagnosis of neurogenic bladder was made. The patient was referred to the Tucson Medical Center for a myelographic study.

Roentgenographic Findings. Myelography revealed a communication between the spinal subarachnoid cul-de-sac situated at about the level of the second segment of the sacrum and a large cavity within the sacrum distal to the cul-de-sac. The communication was extremely small and the opaque medium* could only be made to enter the intrasacral meningocele drop by drop, by judicious coaxing. The abnormal sac accepted the initial 6 cc. of opaque material. The needle was removed and the patient was examined in various positions (Fig. 1, *a–d*). The opaque medium was subsequently coaxed back into the lumbar subarachnoid space and, because of the generous size of the latter, another 6 cc. of opaque medium was added. The lumbar and thoracic segments of the spinal subarachnoid space were then examined and no obvious abnormality identified. Tomograms of the sacrum were then made in the lateral projection and these showed the sacral canal to be markedly widened down to and including the last sacral segment. The anterior sacral wall was quite thin in the region of the fourth and fifth sacral segments. An upright lateral roentgenogram showed a pocket of the sac containing some retained opaque medium to extend slightly outside the sacrum at the level of the distal opening of the sacral canal. It was also noted that the internal structure of this lesion was such that opaque medium became pocketed in various areas.

In retrospect, it is interesting to note findings on an excretory urogram made 6 years prior to this admission. The pyelocalyceal systems and ureters were normal; however, a roentgenogram taken after attempted voiding indicated that only slight emptying of the bladder had occurred. Also, spina bifida occulta of the first 3 sacral segments was noted.

Family History. The patient's 8 year old sister has a congenital hemivertebra of the third lumbar segment on the left. She is asymptomatic at present.

The patient has 2 daughters, one of whom has spina bifida occulta of the fifth lumbar segment. She is asymptomatic.

The patient's father and one aunt (father's side) have had "disk surgery" and were found to have "spinal abnormalities," the exact nature of which could not be ascertained.

Surgical and Pathologic Findings. At surgery the posterior bony wall of the sacrum was found to be paper-thin, but no herniation of the spinal membranes had occurred. Premature rupture of one of the cysts of the apparently multi-chambered lesion occurred during reflection of the overlying musculature. The fluid within the cyst was clear and watery. Careful removal of the sacral roof along with the spinous process of L_5 revealed a large multicystic space, some areas of which could be seen to communicate with the subarachnoid channel. Lying on the left lateral side of the cystic space was a small channel through which elements of the lower sacral nerves could be visualized. An area of tissue was identified as the subarachnoid space where the rootlets of S_3, 4, and 5 emerged. These rootlets passed through their appropriate foramina on the right, but could not be visualized on the left due to displacement by the multicystic mass. The isolated cystic spaces were made to intercommunicate with the spinal subarachnoid space to eliminate further pressure effects; no attempt was made to remove or close the frayed membranes.

Grossly, the specimens removed from the wall of the cystic spaces were composed of white membranous and fibrous bits of tissue. Microscopically the "cyst wall" consisted of a rather loose, somewhat fibrillary laminated fibrocartilaginous tissue, poorly cellular and nearly avascular.

REVIEW OF THE LITERATURE

One of the first reported cases of occult intrasacral meningocele was that of Enderle[6] in 1932. His patient was a 47 year old white female who initially had moderate aching low back pain which, after 1 year, increased rapidly in severity and radiated down the posterior surface of both thighs. When examined, the patient was tender over the lumbosacral vertebral spines and paravertebral areas. Roentgenograms of the lumbosacral spine revealed an increase in the size of the sacral hiatus and lumbarization of the first sacral segment. Myelography showed nothing abnormal at first. However, a delayed roentgenogram taken 24 hours later revealed a collection

* Pantopaque.

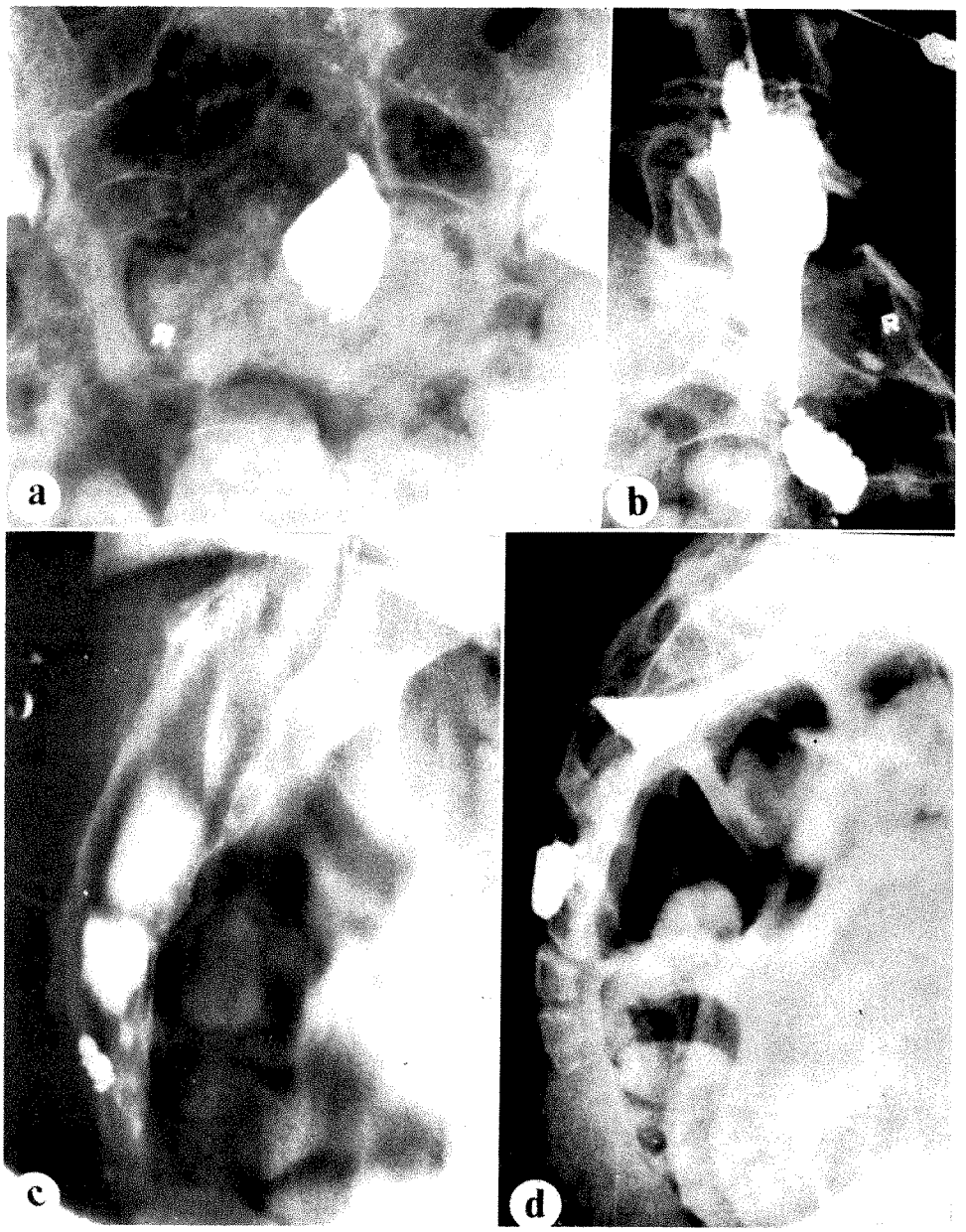


FIG. 1. (*a*) Anteroposterior view of sacrum after 6 cc. of opaque material had entered the intrasacral meningocele. (*b*) Prone view after another 6 cc. of opaque material had been introduced into the lumbar subarachnoid space. Note the narrow isthmus by which the cul-de-sac communicates with the intrasacral sac. (*c*) Lateral tomogram of sacrum. There is 12 cc. of opaque material contained in the intrasacral meningocele, composed of intercommunicating chambers. Note some of the opaque material immediately beneath the skin at the sacral hiatus. Note also the paper-thin anterior sacral wall at the third and fourth sacral segments. (*d*) Upright lateral view of sacrum showing opaque material pooled in two pockets of the intrasacral meningocele, one pocket subcutaneously at sacral hiatus.

of opaque material within a widened sacral canal, connected to the lumbar sac by a narrow isthmus. Enderle determined that it was composed of both the dura and arachnoid membranes and proposed that it be named "occult intrasacral meningocele."

In 1932 Wilson and Wakeley[17] reported a

case in which the outstanding presenting symptom was that of excruciating radicular and local pain. It is also interesting to note that there was no exterior deformity or anomaly and no symptoms were present until the age of 16 years.

Archer, Cooper and Cimmino[2] reported 3 cases in 1948. Their 3 cases presented with differing symptoms and signs: gradually increasing pain, pain following trauma and urinary incontinence. They proposed a differential diagnosis which included both intradural and extradural tumors. It will suffice here to say that neoplasms in this area are more common than occult intrasacral meningocele and can produce the same symptoms.

Baker and Webb[3] reported a case of a 28 year old female with a 10 year history of gradually increasing "sciatic pain" and stiffness finally becoming continuous and severe enough to prevent her from working. Physical examination revealed moderate lumbosacral tenderness and absence of the left ankle reflex and a weakened reflex on the right. Fortunately for the patient, a sacral laminectomy with ligation of the dura and arachnoid at the normal level was followed by an almost complete abatement of symptoms. These authors point out that perineural cysts of sacral nerve roots are smaller and have a distinctly perineural location which is not the case in occult intrasacral meningoceles.

Pool[14] presented 2 cases. The first, a 40 year old woman, had experienced slow progression (18 years, duration) of pain and paresthesias in the left hip and thigh, followed by urinary frequency (10 years) and finally incontinence. At surgery she was found to have an abnormally long spinal cord extending down through the sacral meningocele where it was subjected to direct compression by an associated intradural lipoma. The second case, a 30 year old male, exhibited a spastic paraparesis and sensory signs as high as T8, reflecting indirect spinal cord changes apparently due to tension transmitted to the cord from the sacral meningocele by a tight filum terminale. Both of these patients had symptoms of lumbar and sacral nerve root involvement represented by pain or altered sensation in one or both legs, bladder and rectal dysfunction, and sexual impotence. Trauma initiated the onset of symptoms and signs in each case (childbirth in one, jeep riding and heavy lifting in the other). Pool[14] points out that multiple sclerosis or the late effects of poliomyelitis may be mimicked. Therefore, roentgenographic studies of the sacral canal should be considered in such cases. Pool also mentions that surgical intervention should be carried out promptly when this diagnosis is made, in order to prevent irreversible nerve root and spinal cord changes.

Although occupying both the upper sacrum and lower lumbar area, one of Walker's[16] cases of "vertebral canal dilatation" may be included in our review. It qualifies because the main dilatation, 4 cm. in diameter, was in the sacrum and was completely enclosed within the bony canal. His patient was a 25 year old male who complained of a deformed left leg, paresthesias in the saddle region, and urinary incontinence. Physical examination and testing revealed an atrophic left leg, bilateral sacral hypoesthesia, and neurogenic bladder; dilatation of the sacral canal was noted on roentgenograms, and at operation a lipoma of the conus medullaris adherent to the coccyx (abnormally low position) was found within the meningocele cavity. It will be noted that this case is very similar to the second case of Pool mentioned above.

Palazzoli[12] has reported a case that fits the definition but differs in make-up and tissue involvement. He also has put forth considerable effort to establish an embryologic calendar of events and natural mechanisms which set the stage for this and other "dysrhaphic states." His patient was a 21 year old female who experienced a violent exacerbation of her previously episodic lumbosacral pain 5 years prior to the hospital admission. After the onset of



FIG. 2. From Palazzoli's[12] paper. Upright roentgenogram taken 1 hour after introduction of opaque material into the subarachnoid space. It shows that "the mass of iodized oil communicated through a short filiform channel with 2 underlying sacs, in the lower of which it was uniformly distributed, whereas in the upper one it was distributed in a nonhomogeneous manner."

more severe pain she also had radiation of pain down one leg to the heel. Interestingly, she was almost completely relieved of her pain when lying down and had increased pain when she coughed or laughed, as well as during defecation. Later when she was operated upon, a very mobile cerebrospinal fluid-filled sac was found within a normal size sacral canal. The variability of the symptoms with position and intra-abdominal pressure could then be explained by increased filling of the sac with cerebrospinal fluid when the patient was standing which, in turn, caused pressure and tension on the spinal nerve roots. When in the recumbent position, the sac's narrow stalk (Fig. 2) and mobile nature allowed a larger outlet and the fluid drained, thus relieving pressure on the nerve roots. Another significant finding suspected during surgery and apparently proved microscopically was that the meningocele sac was composed entirely of arachnoid and did not involve the dural layers. The arachnoid sac appeared to have herniated out of a defect in the dural envelope. This could shed some light on the possible mechanism of formation and also suggests the possibility of the existence of different types of occult intrasacral meningoceles.

Howieson and co-workers[8] have described 3 cases of subarachnoid expansions of the sacral canal. (They prefer not to use the term "occult sacral meningocele.") One patient, a 51 year old female, suffered from progressive weakness of one leg. She had suffered various pelvic, gastroenteritic and urinary complaints and had undergone numerous abdominal and pelvic operations. Myelography showed a large intrasacral expansion of the subarachnoid space. "The expanded region was remarkable in that it appeared to arise from the terminal tapered part of the subarachnoid space which then opened into a large cyst-like expansion." Another patient, a 74 year old man, suffered from urinary and fecal incontinence and anesthesia in the saddle area for several months. Myelography showed a "rounded elongated dilatation of the sacral subarachnoid space which filled readily with pantopaque."

Case 9 from the article on perineural sacral cysts by Abbott and co-workers[1] would seem to fit more easily into the category of occult sacral meningoceles. This was also the opinion of the authors as evidenced by their statement, "Sections of the cyst have failed to disclose any nerve fibers in its structure. For this reason, and because of its gross appearance, it may be that it is an intrasacral meningocele . . ." The patient was a 28 year old female who had suffered from urinary and rectal incontinence since childhood as well as from weakness of the lower extremities since 16 years of age. Roentgenograms of the sacrum revealed a very large sacral

canal with thinning of the posterior bony plate. At myelography it was noted that there was a small opening between the cyst and the cul-de-sac of the normal lumbosacral leptomeninges.

Heppner and Diemath[7] reported a case which resembles that of Palazzoli in some respects. A valve-like effect was found to be responsible for intermittent pain resulting from cerebrospinal fluid in a "long-stalked protruding sac of the spinal meninges." At surgery this sac was found in the upper lumbar area of the cord and, therefore, it does not qualify as an occult intrasacral meningocele. Their discussion covers "spinal extradural cysts" which are usually found in the thoracic portion of the neural canal. These authors reviewed 36 cases in the literature and, after carefully studying their own cases, concluded that these cysts, whether connected with the subarachnoid space or not, are always composed of meningeal membranes. This, they argue, qualifies them as meningoceles. Their discussion of modes of formation is compatible with that of Palazzoli and both will be reviewed.

Although there are not enough cases on record at this writing for a statistical evaluation, the following symptoms and signs appear to be most common: (1) urinary retention or incontinence; (2) "lower motor neuron" signs—commonly, reduction of ankle jerks; (3) progressive pain in a sciatic distribution or sacral and/or lumbar area pain, which may follow trauma; (4) sensory impairment in the "saddle area"; and (5) spina bifida occulta.

Less commonly encountered are the following: (1) "upper motor neuron" signs; (2) rectal dysfunction; (3) leg muscle atrophy; and (4) transitional vertebra.

Findings such as a dermal sinus, sacrococcygeal dimple (coccygeal vestige area), sacral hypertrichosis, pigmentation, or subcutaneous lipoma[10] quite commonly accompany this defect.

Anteroposterior and lateral roentgenograms of the sacrum usually show a widening of the bony sacral canal and thinning of the anterior and posterior walls. Myelography will usually demonstrate a narrow canal connecting the subarachnoid cul-de-sac with the meningocele cavity. Some authors emphasize the importance of leaving the opaque medium in the subarachnoid space for at least 48 hours and taking delayed roentgenograms.

In some cases the neurologic findings may mimic those seen in degenerative diseases of the nervous system, such as multiple sclerosis. Other etiologic entities to be considered included neoplastic disease, inflammatory disease and disk lesions.

THEORIES OF CAUSATIVE FACTORS

Occult intrasacral meningoceles fit somewhere in the broad spectrum of anomalies ranging from spina bifida occulta and dermal sinus to total craniorachischisis and anencephaly. Exactly where this entity does fall is not clear. Traditionally, most of these anomalies have been attributed to a failure of closure of the neural tube or surrounding mesoderm following developmental arrests at various times during embryogenesis.

Von Recklinghausen[15] can be credited with advancing this idea when he noted an open neural tube in an embryo during microscopic examination. Although there are now some strong critics of the developmental arrest and failure-of-closure theory, as will be mentioned later, there has been a good deal of research which supports it. As reviewed by Campbell,[4] the concepts of organizer substances and induction have been put to the test by investigators using chemical and physical agents on animal embryos to produce spinal anomalies similar to those seen in humans. It appears that proper neural induction is dependent upon normal development of mesoderm. Campbell states: "Possibly the factors producing these abnormal inductions under experimental conditions may exist in the form of mesodermal deficiencies in the human embryo when faulty neural induction leads to hydromyelia and myelo-

meningocele. In other words, clinical lesions ranging from a minor neural malformation associated with bifidism of the neural axis to complete rachischisis of the spinal column with dysraphism, or anencephaly, will depend upon the degree to which the mesenchyma is defective and, therefore, incapable of proper neural induction."

A proliferative element in cases of myeloschisis has been noted and discussed by Patten.[13] He carefully analyzed the developmental process in myeloschisis as displayed by three human embryos and a term rabbit fetus. A comparison of the neural cell mass was made using a grid sizing technique and it was noted that more neural plate tissue was present in the open malformed area than in adjacent normal cord. "Furthermore, the extent of the neural plate tissue appeared greater than normal in relation to other surrounding structures."

Patten contends that the open neural tube may be the result of local overgrowth which interferes with closure, rather than the result of a "developmental arrest" which left the tube unclosed because of too little growth of the neural folds. This observation is not at complete odds with the "improper induction" idea, since the mesoderm underlying the neural ectoderm could feasibly cause a "proliferation" as well as an "arrest."

It was also noted, primarily in the rabbit specimen, that although there was an atrophic epidermis in the marginal zone around the defect, there was a tremendous increase in subcutaneous vascularity. This discovery may have some relation to hydromyelic theories mentioned below.

Patten mentions that other conclusions related to the timing of these developmental processes may be drawn:

1. A spina bifida co-existing with myeloschisis is secondary to it.
2. A spina bifida occulta must arise independently much later in development as a result of factors regulating growth of the vertebrae themselves.
3. "A meningocele with little involvement of the cord may well be a sequel to a primary spina bifida in which the unclosed neural arches invited the herniation of fluid-dilated meninges."

He considers the latter a much more "tentative conclusion."

Admittedly, little has been said in the foregoing paragraphs to suggest a mechanism for formation of an intrasacral meningocele, with the possible exception of the last statement (number 3 above). However, there is some evidence which may suggest that increased cerebrospinal fluid pressure may be related to the genesis of all these defects including the intrasacral meningocele. Gardner[6] reminds us that this is not a new theorem, as Morgagni,[11] 200 years ago, postulated that cerebrospinal fluid pressure transmitted from the embryo's ventricular system was responsible for disruption of the vertebral canal and spinal membranes. Before discussing the effects of hydromyelia, it will be helpful to relate some developmental data.

Palazzoli[12] discusses the differences in the modes of formation of the spinal cord at different levels. He points out that the lower lumbar and sacral segments of the spinal cord are formed by a more complex mechanism than are the thoracic and cervical segments. Initially, a solid cord of cells differentiates from the cellular group constituting the primitive streak. Later this cord is canalized, and the lumen formed becomes continuous with the thoracic spinal cord above. At the caudal extremity another type of mechanism obtains. Here the central canal originally is subdivided into 2, 3, or 4 secondary canaliculi, which either merge into a single canal and then become obliterated or persist into the adult stage. The caudal end of the neural tube thus formed gives rise to the filum terminale, which undergoes thinning of its walls and reduction of its lumen with the exception of a terminal sinus at its distal extremity. The posterior

wall of this terminal sinus extends to the surface as the posterior neuropore, which usually degenerates and is occluded.

From the fifth to the eleventh week of embryogenesis, when the embryo is from 25 to 53 mm. in crown-rump length, the malformational processes seem to be of the greatest interest, since they are compatible with postnatal life. As opposed to earlier periods, when defective development occurred and necessarily caused mesodermal and ectodermal dysrhaphism in an "associated dysrhaphic state" (*e.g.*, cranio-rachischisis), the changes referable to the third period can exist alone or in various associations. This is to say, that the "dissociated dysrhaphic state" can occur, an example of which is a combination of spina bifida occulta, sacral hypertrichosis and a meningocele, *not* necessarily accompanied by a primary alteration in the spinal cord or its roots.

Therefore, Palazzoli maintains that the defects responsible for the occult intrasacral meningocele occur between the fifth and eleventh week and can exist because the caudal extremity of the spinal cord in the human embryo forms in a different fashion which allows early (before 4 weeks) separation of the cutaneous ectoderm from the neural ectoderm. In his patient the meningocele sac was composed entirely of arachnoid membrane and, thus, it appeared that incomplete formation of the dura had "invited" a herniation of the more delicate arachnoid, possible under physiologic hydromyelia pressure.

It is now apparent that all occult intrasacral meningoceles are not the same and many involve the dura and some of the filum terminale tissue proper, and not just the meninges. Certainly, microscopic differentiation of the layers involved should be attempted, but the end result of many of these defects is replacement by fibroblasts and their product, connective tissue.

In Keen's article[9] the author develops a "hydrops pressure theory" which maintains that all congenital deformities allied to spina bifida and anencephaly can be explained through disturbances of the cerebrospinal fluid mechanism and the effect of increased pressure. The increased pressure can "destroy nerve tissue, split open the dorsal roof plate and the dorsal coverings of the neural tube, if the pressure is of the internal hydrocephalic type; or only the dorsal coverings if the pressure is of the external hydrocephalic type."

More recently Gardner[6] has drawn attention to the physiologic hydrocephalomyelia in the normal embryo. This physiologic distention is usually compensated by leakage of fluid out of the "attenuating rhombic roof" which dissects open the subarachnoid space. If this flow is impeded by failure of (or late) perforation of the communicating foramina or inadequate diffusion across membranes prior to rupture, a transient pathologic hydrocephalomyelic condition will exist. The central canal of the cord narrows normally because the foramina of Luschka and Magendie are patent and, therefore, the pressure in the central canal and ventricular system is relieved and transmitted to the subarachnoid space. However, if there is no venting accompanied by inadequate diffusion, the central canal will dilate. This sets the stage for many types of defects. If the internal pressure is just under the bursting pressure, a myelocele, syringomyelia, or Klippel-Feil syndrome may ensue. If the neural tube bursts, a myeloschisis or total rachischisis occurs. If the pressure is not so high as to cause permanent distortion of the cord, the precartilage cells and meningeal primordia are stretched and thus the sclerotomal elements may fail to unite or take a "permanent set." It will be recognized that the latter situation may account for a sacral precartilage tissue dilatation. Even if the cerebrospinal fluid pressure is vented from the central canal in a normal manner, if a pathologic rise in pressure occurs shortly thereafter, the dura and arachnoid would be stressed and caused to "balloon out," possibly in the sacral region, causing displacement of the precartilage cells. If this condition were not completely re-

versible, a meningocele sac would remain inside a dilated sacrum.

If the genesis of a dilated or open neural canal is ascribed to a pathologic hydrostatic effect, why are the lesions so localized? This may be answered by considering that there is a rostral to caudal maturation of the spine and enclosed neural elements. Therefore, the timing of a transient rise in cerebrospinal fluid pressure is important, as this rise could occur during a development period of least strength at a given level. The narrow neck connecting an intrasacral meningocele with the dural cul-de-sac could be accounted for by the subsequent disproportional growth rates of the vertebrae and spinal cord.

The hydromyelic theory is definitely in the field of "arm chair philosophy" and is presented because a cerebrospinal fluid pressure disturbance does appear to lend itself to the morphology of the intrasacral meningocele. Definitive laboratory work is needed to prove or disprove these theories. Actually, the best laboratory effort appears to have been directed to support the hyperplasia theory[13] associated with an improper mesodermal inductive process. Since a multicystic and loculated effect was seen in the case presented (as well as others), which does suggest a hyperplasia of meningeal tissue, this mode should be kept in mind as an equally plausible method of formation.

Another reasonable and perhaps simpler mode of development was suggested by Enderle.[5] In the fetus the dural sac and neural tube reach beyond the coccyx to the so-called filum caudale. Subsequently the neural tube loses its connection with the filum caudale and begins to retract, remaining connected with its extremity by means of the filum terminale which runs from the conus terminalis medullae to the forca coccigea (coccyx bones). The dural sac is then constricted in its principal width around the filum terminale until it reaches, in the 9 cm. fetus, almost the disposition which is found in the adult. Therefore, a pathogenic agent could disturb fetal development before this time, that is, as long as the full meningeal sac accompanies the neural tube down to the region of the coccyx. If the ascent of the meningeal sac had been arrested, it would have remained in its primitive state, whereas the spinal cord (assuming it did not fail to ascend) would have continued to develop normally, with retraction in the usual manner. This is a pure developmental arrest and if there is little bony involvement, as does occur in some cases, it explains the defect quite adequately. Whether or not the mere presence of a fluid-filled meningeal sac in the sacral precartilage region would account for a widened bony canal in the adult is again purely speculative. In the child or adult a "pressure atrophy" of the bony sacral canal produced by hydrostatic pressure transmitted through the walls of the meningocele is another good possibility.

CONCLUSION

A differential diagnosis of patients with lumbosacral, sciatic, or urinary tract symptoms must include spinal developmental defects, including the rare, elusive occult intrasacral meningocele. Clues to significant pathologic change within the neural canal are provided by bone, soft tissue, and skin abnormalities anywhere in the lumbosacro-coccygeal region. Anteroposterior and lateral roentgenograms of the pelvis may provide information by revealing a widening and thinning of the sacral neural canal. A myelographic study should follow if there is an abnormal roentgenogram or, as in some cases reviewed here, if symptoms and/or signs persist in spite of treatment.

SUMMARY

A rare case of occult intrasacral meningocele is presented, the literature reviewed, symptoms and findings tallied, and possible etiologies explored.

This congenital defect is a dilated sac, composed of the meninges lying wholly in an enlarged, thin-walled sacral canal and connected with the subarachnoid cul-de-sac

above by a narrow cerebrospinal fluid channel.

Symptoms referable to the low back, lumbosacral spinal nerves and urinary tract may mimic those of intervertebral disk syndrome, spinal canal neoplasms, inflammatory lesions and degenerative neurologic disease.

Clues to underlying congenital defects within the spinal canal are skin changes (*e.g.*, pilonidal sinus), soft tissue abnormalities (*e.g.*, subcutaneous lipoma), and bone defects (*e.g.*, spina bifida occulta).

Possible etiologies range from a simple developmental arrest to theories involving cerebrospinal fluid pressure effects on the formation of the spinal cord and meninges

André J. Bruwer, M.D.
Tucson Medical Center
P. O. Box 6067
Tucson, Arizona 85716

We are indebted to Robert E. Asnis, Ph.D., of Drexel Hill, Pennsylvania, for translations of the articles by Heppner and Diemath,[7] by Enderle[5] and by Palazzoli;[12] and to the Tucson Hospitals Medical Education Program for covering the cost of translation. We also wish to thank Doctor George Nash, neurosurgeon, and the Tucson Medical Center for permission to publish this case report. Lastly, one of us (A.J.B.) would like to make the comment that, in the drive for recruitment of medical students into the field of radiology, externship programs be encouraged. Doctor Young started work on this paper as a project during an externship at the Tucson Medical Center Department of Roentgenology, between his junior and senior years at Northwestern Medical School. For the junior author (A.J.B.) this was a stimulating experience.

REFERENCES

1. Abbott, K. H., Retter, R. H., and Leinbach, W. H. Role of perineurial sacral cysts in sciatic and sacrococcygeal syndromes: review of literature and report of nine cases. *J. Neurosurg.*, 1957, *14*, 5–21.
2. Archer, V. W., Cooper, G., Jr., and Cimmino, C. V. Occult meningocele of sacrum: report of three cases. *Radiology*, 1948, *51*, 691–695.
3. Baker, G. S., and Webb, J. H. Intrasacral meningocele causing backache and sacral nerve pain: report of case. *Proc. Staff Meet. Mayo Clin.*, 1952, *27*, 231–234.
4. Campbell, J. B. Congenital anomalies of neural axis: surgical management based on embryologic considerations. *Am. J. Surg.*, 1948, *75*, 231–256.
5. Enderle, C. Meningocele intrasacrale occulto (rivelato con la mielografia). *Riv. neurol.*, 1932, *5*, 418–423.
6. Gardner, W. J. Embryologic origin of spinal malformations. *Acta radiol.* (Diag.), 1966, *5*, 1013–1023.
7. Heppner, F., and Diemath, H. E. Gibt es Meningozelen bei geschlossenem Wirbelkanal? *Zentralbl. Neurochir.*, 1960, *20*, 227–235.
8. Howieson, J., Norrell, H. A., and Wilson, C. B. Expansion of subarachnoid space in lumbosacral region. *Radiology*, 1968, *90*, 488–492.
9. Keen, J. A. Genesis of spina bifida and allied congenital defects. *Clin. Proc.*, 1948, *7*, 162–172.
10. Lassman, L. P., and Michael James, C. C. Lumbosacral lipomas: critical survey of twenty-six cases submitted to laminectomy. *J. Neurol., Neurosurg. & Psychiat.*, 1967, *30*, 174–181.
11. Morgagni, J. B. The Seats and Causes of Diseases Investigated by Anatomy. Volume III. Translated from the Latin by B. Alexander, A. Millar and T. Cadell, London, 1769.
12. Palazzoli, A. Rilievi clinici e patogenetici su un caso di meningocele sacrale occulto simulante un'ernia discale. *Bol. Soc. Medico Chir.*, 1963, *17*, 203–225.
13. Patten, B. M. Embryological states in establishing of myeloschisis with spina bifida. *Am. J. Anat.*, 1953, *93*, 365–395.
14. Pool, J. L. Spinal cord and local signs secondary to occult sacral meningoceles in adults. *Bull. New York Acad. Med.*, 1952, *28*, 655–663.
15. von Recklinghausen, F. D. Untersuchungen über die Spina bifida. *Arch. path. Anat.*, 1886, *105*, 243, 373.
16. Walker, A. E. Dilatation of vertebral canal associated with congenital anomalies of spinal cord. Am. J. Roentgenol. & Rad. Therapy, 1944, *52*, 571–582.
17. Wilson, S. A. K., and Wakeley, C. P. G. Occult lumbosacral meningocele. *J. Neurol., Neurosurg. & Psychiat.*, 1932, *13*, 45–49.

SCHISTOSOMIASIS OF THE SPINAL CORD*

By ARNOLD CHAIT, M.D.,† *and* WILLIAM E. GANNON, M.D.
BROOKLYN, NEW YORK

DURING the past several years the diagnosis of schistosomiasis mansoni has been made with increasing frequency in the eastern United States. The disease, once a rarity in this country, must now be considered in patients of Puerto Rican origin who present with symptoms related to the gastrointestinal tract or those suggesting portal hypertension, chronic lung disease, and cor pulmonale. Roentgenographic observations at this institution of the involvement of multiple organ systems by this parasite have been previously discussed.[6] We have recently had the opportunity to observe 2 patients presenting with transverse myelitis as an unusual manifestation of schistosomiasis. Only two similar cases have been reported in Puerto Rico,[15] where it is conservatively estimated that 10 per cent of the population is infected.[21] The only previous case diagnosed in life on the North American continent was reported in 1952 in a patient from Venezuela.[19]

REPORT OF CASES

CASE I. I.S., a 51 year old former sugar cane worker who had come to the United States from Puerto Rico 2 years previously was admitted to a neighboring hospital on March 5, 1963. He had been well until 2 days prior to admission when he felt his legs suddenly buckle beneath him while climbing stairs. Thereafter he remained paraplegic and incontinent of urine. On March 26, 1963, he was transferred to Kings County Hospital with a tentative diagnosis of spinal cord tumor. On admission, flaccid paraplegia was present; no reflexes were elicited in the lower extremities. Reflexes were present in the upper, but absent in the lower abdomen. There was hypesthesia from the iliac crest to the mid-thigh level and complete anesthesia from the mid-thigh downward. The sensory level was interpreted as being at T-11. He was incontinent of urine, and findings on cystography were those of neurogenic bladder. An exploratory laminectomy performed from T-7 to T-12 on March 28, 1963 demonstrated no abnormality save for an area of diminished vascularity at the T-11 area and engorged veins above and below this region. No satisfactory diagnosis was made until August, 1963 when an alert house officer, having recently read a review by Marcial-Rojas and Fiol,[15] suggested the possibility of schistosomiasis. A rectal valve biopsy on August 30, 1963 was indeed positive for schistosomiasis. During the months following laminectomy, the patient developed intractable pain in the lower back, knees and feet.

The diagnosis of schistosomiasis of the spinal cord has not been histologically confirmed in this patient. It appears reasonable, however, to attribute the transverse myelitis and radiculitis to schistosomal involvement. Venous thrombosis and congestion of the veins of the leptomeninges, probably present in this case, have been described in schistosomiasis of the spinal cord.[14] It is worth commenting that even in a hospital in which schistosomiasis figures prominently in many differential diagnoses, 4 months elapsed before this diagnosis was considered.

CASE II. G.D., a 20 year old Puerto Rican male was admitted to the Kings County Hospital on April 24, 1967. He remembered having heard a 'snap" in his back 2 weeks previously, followed by progressive weakness and bilateral lumbosacral pain. During the week preceding admission he was unable to walk without support. He had had no difficulty in voiding until the day of admission. On admission there was marked weakness of hip flexion and extension, of knee flexion, and of dorsiflexion of the feet. Plantar flexion of the feet was mildly reduced. The knee jerk reflex was absent bilaterally and the ankle jerk diminished on the right. There was hypalgesia to 1 inch above the groin bilaterally. Sacral sensitivity was diminished on the right. The bladder was distended. Rectal tone was present. Myel-

* From the Department of Radiology of the Kings County Hospital Center, and the Downstate Medical Center of the State University of New York, Brooklyn, New York.
† Present Address: Department of Radiology, Presbyterian-University of Pennsylvania Medical Center, Philadelphia, Pennsylvania.

ography demonstrated an intramedullary mass at T-11 to T-12 (Fig. 1 and 2). At laminectomy a "tumor" of the conus medullaris was found. On biopsy, this was demonstrated to contain perivascular and interstitial granulomatous inflammatory tissue in which schistosome ova were seen. Postoperatively, paraplegia became more pronounced with a sensory level at T-12 to L-1. A few days later, stool specimens were found to contain schistosome ova.

In this case, although schistosomiasis was readily confirmed at biopsy, the diagnosis was not entertained prior to laminectomy.

DISCUSSION

The myriad manifestations of schistosomiasis have long been recognized in areas of the world in which this parasite is endemic. In this age of rapid transportation and population mobility, it has become necessary for physicians in nonendemic regions to be equally familiar not only with the more common aspects of this disease but with its more bizarre manifestations as well.

In 1963, Marcial-Rojas and Fiol[15] reviewed the world literature concerning the neurologic complications of schistosomiasis. They were able to find 95 such cases reported, 25 of which demonstrated spinal cord involvement. Nineteen of the latter cases were histologically proven. These authors added 2 cases of their own presenting with transverse myelitis. Since the appearance of this review article, a total of 14 more cases of schistosomiasis of the spinal cord has appeared, 6 of which have been histologically proven.[1,3,4,5,11,20] The present 2 cases bring the total to 43, 28 of which are histologically confirmed. Our cases are the fourth and fifth reported on the North American continent.

Man becomes involved in the life cycle of the schistosome fluke when infected by the fresh water, free swimming cercarial form which may penetrate intact skin. The larvae migrate to the right side of the heart via systemic veins or lymphatics, and pass through the lung capillaries to enter the systemic circulation. It is the usual theory that only those larvae which

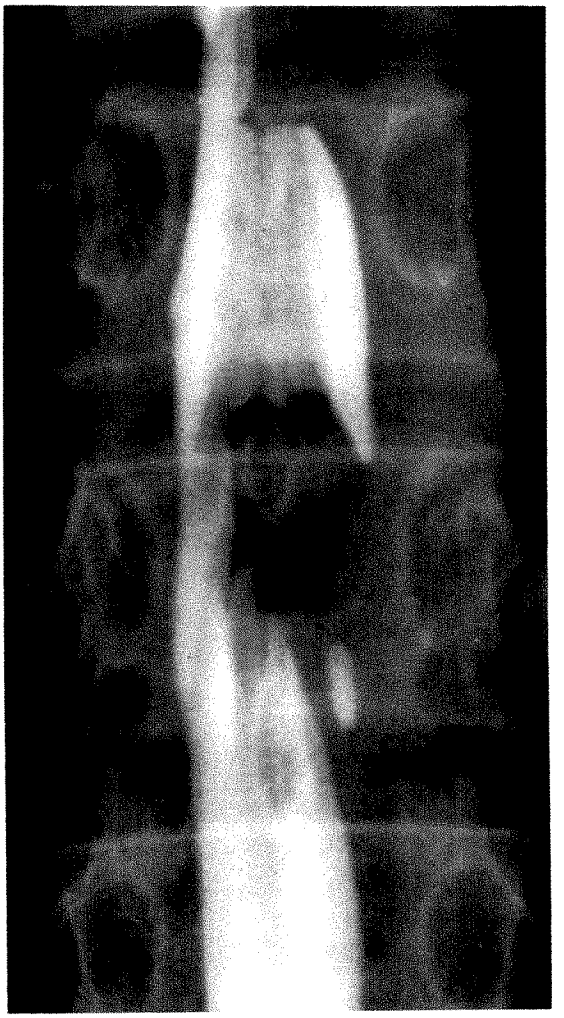


FIG. 1. Case II. Anteroposterior spot roentgenogram reveals widening of the translucent shadow of the spinal cord, in the region of T-11 to T-12.

are distributed to the portal venous system reach maturity and mate. In the case of the species mansoni, the adult female deposits its ova in small colonic or rectal venules. Those ova which reach the visceral lumen and are ejected into fresh water containing the appropriate snail intermediate host continue the life cycle.[9,12,17] It is the "unsuccessful" ova which create the picture with which we are familiar. Granulomatous changes are found principally in the colon but have also been reported in other parts of the gastrointestinal tract. Hepatic cirrhosis is a frequent

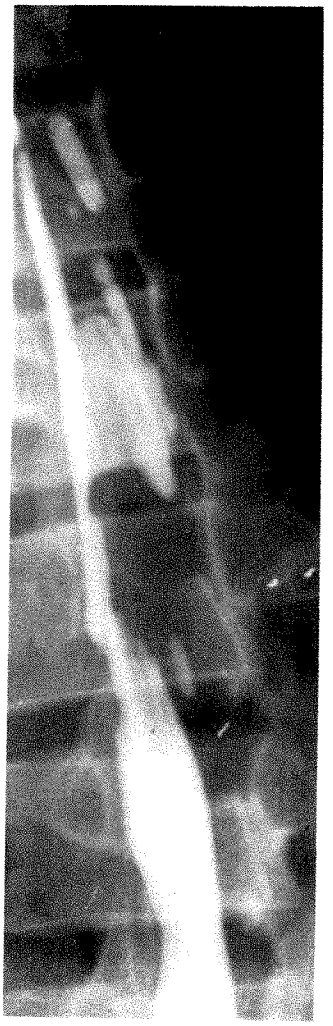


FIG. 2. Case II. Oblique spot roentgenogram again shows the enlargement of the radiolucent shadow of the spinal cord in the same area.

eventual sequela of granulomatosis of the liver.[13] In the event that cirrhosis does occur, the portal-systemic shunts hereby formed, involving the esophageal veins, paravertebral veins, and the azygos system, form a potential route for the arrival of ova in the lungs,[2] leading to chronic lung disease and cor pulmonale. Hepatic cirrhosis also encourages the opening of portal systemic venous shunts in the hemorrhoidal plexus, but is not a prerequisite for shunting at this level. It is probable that during every act of coughing in the normal, the hemorrhoidal venous plexus shunts freely

It has also been suggested that owing to anastomoses between the sacral plexus and the inferior arachnoid plexus and to pressure changes during the act of defecation, there is continuous migration from the rectal veins to the lower spinal cord.[10]

Schistosomiasis of the spinal cord must be considered an "ectopic" lesion in that the vessels of the spinal cord are not generally utilized by the adult worm, larva, or ovum. Faust[8] has advanced several theories to account for the presence of ectopic lesions. The most generally accepted theory makes use of the above mentioned collaterals between the portal system and the vertebral venous system. More ingenious explanations suggest transpulmonic arterial embolization of ova made possible by pulmonary arteriovenous fistulae created by schistosome granulomata in the lung.[7] In the presence of a patent foramen ovale, passage of ova from systemic veins to systemic arteries can be readily understood. There are indeed those who believe that larvae may mature and oviposit outside the portal bed.[16] Some support for this latter theory may be assumed from the clustering of ova found in the spinal cord in several reported cases of schistosomiasis, suggesting that they were deposited *in situ*. There is one report of invasion of the spinal cord by an adult fluke.[18]

Although few reports of schistosomiasis of the spinal cord have appeared, it is probable that this lesion is more frequently present than suspected. Several reports of schistosomiasis of the spinal cord have been made from autopsy material in patients who clinically were entirely asymptomatic.[5] Indeed, the affected spinal cord may appear, even on histologic section, grossly normal. In at least 1 reported case, there was not even a tissue reaction about the ova.[5] On the other hand, there may be signs of transverse myelitis with (Case II) or without (Case I) granulomatous tumor. Cases of transverse myelitis with normal appearing myelograms have been reported.[3,4] Frequently, as in our cases, radiculitis may become a major problem.[4]

SUMMARY

Two cases of intramedullary schistosomiasis are reported, one proven and one assumed, representing the fourth and fifth such reports from this continent. The histologic lesion is one of granulomatous reaction and vasculitis, and the roentgenographic finding is that of an intramedullary mass on myelography. Transverse myelitis is the usual sequela and radiculitis is frequently a significant co-existing problem.

Arnold Chait, M.D.
Department of Radiology
Presbyterian-University of Pennsylvania
Medical Center
51 North 39th Street
Philadelphia, Pennsylvania 19104

REFERENCES

1. Barnett, A. M. Bilharzial granuloma of spinal cord. *South African M. J.*, 1965, *39*, 699–700.
2. Batson, O. V. Function of vertebral veins and their role in spread of metastases. *Ann. Surg.*, 1940, *112*, 138–149.
3. Bird, A. V. Acute spinal schistosomiasis. *Neurology*, 1964, *14*, 647–656.
4. Bird, A. V. Spinal cord complications of bilharziasis. *South African M. J.*, 1965, *39*, 158–162.
5. Budzilovich, G. N., Most, H., and Feigin, I. Pathogenesis and latency of spinal cord schistosomiasis. *A.M.A. Arch. Path.*, 1964, *77*, 383–388.
6. Chait, A. Schistosomiasis mansoni: roentgenologic observations in nonendemic area. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1963, *90*, 688–708.
7. deFaria, J. L. Pulmonary arteriovenous fistulas and arterial distribution of eggs of Schistosoma Mansoni. *Am. J. Trop. Med.*, 1956, *5*, 860–862.
8. Faust, E. C. Inquiry into ectopic lesions in schistosomiasis. *Am. J. Trop. Med.*, 1948, *28*, 175–199.
9. Faust, E. C. Schistosomiasis. In: A Textbook of Medicine. Eighth edition. Edited by R. L. Cecil and R. F. Loeb. W. B. Saunders Company, Philadelphia, 1951, pp. 410–414.
10. Gama, C. Compression granuloma of spinal cord caused by schistosoma mansoni ova; epiconus; conus medullaris; cauda equina: report of case. *J. Int. Coll. Surgeons*, 1953, *19*, 665–674.
11. García-Palmieri, M. R., and Marcial-Rojas, R. A. Protean manifestations of schistosomiasis mansoni: clinicopathological correlation. *Ann. Int. Med.*, 1962, *57*, 763–775.
12. Koppisch, E. Diseases due to trematodes. In: Pathology. Edited by W. A. D. Anderson. C. V. Mosby Company, St. Louis, 1948, pp. 417–425.
13. Koppisch, E. Studies on schistosomiasis mansoni in Puerto Rico. VI. Morbid anatomy of disease as found in Puerto Ricans. *Puerto Rico J. Pub. Health & Trop. Med.*, 1941, *16*, 395–455.
14. Maciel, Z., Coelho, B., and Abath, G. Myélite schistosomique due au S. Mansoni: étude anatomo-clinique. *Rev. Neurol.*, 1954, *91*, 241–259.
15. Marcial-Rojas, R. A., and Fiol, R. E. Neurologic complications of schistosomiasis: review of literature and report of two cases of transverse myelitis due to S. mansoni. *Ann. Int. Med.*, 1963, *59*, 215–230.
16. Middlemiss, H. Schistosomiasis. In: Tropical Radiology. Edited by H. Middlemiss. Intercontinental Medical Book Corporation, New York, 1961, pp. 98–103.
17. Porter, R. J. Human blood flukes. In: Jordan-Burrows Textbook of Bacteriology. Fifteenth edition. Edited by W. Burrows. W. B. Saunders Company, Philadelphia, 1949, pp. 791–793.
18. Raper, A. B. Cerebral schistosomiasis. *East African Med. J.*, 1948, *25*, 262–263.
19. Ross, G. L., Norcross, J. W., and Horrax, G. Spinal cord involvement by schistosomiasis mansoni. *New England J. Med.*, 1952, *246*, 823–826.
20. Wakefield, G. S., Carroll, J. D., and Speed, D. E. Schistosomiasis of spinal cord. *Brain*, 1962, *85*, 535–552.
21. White, P. C., Jr., Pimentel, D., and Garcia, F. C. Distribution and prevalence of human schistosomiasis in Puerto Rico in 1953. *Am. J. Trop. Med.*, 1957, *6*, 715–716.

EFFECT OF PARABENS ON THE PERMEABILITY OF THE BLOOD: BRAIN BARRIER TO WATER-SOLUBLE RADIOPAQUE MEDIA*

By WILLIAM H. STRAIN, PH.D., ROBERT J. RIVERS, JR., M.D., RICHARD J. O'REILLY, M.D., DANIEL T. DANAHY, M.D., MARTIN R. THOMAS, M.D., *and* ROBERT M. WILSON
ROCHESTER, NEW YORK

INCREASINGLY large amounts of water-soluble radiopaque media are being used each year in roentgenographic examinations. These agents are employed in a large percentage of the estimated 100,000 procedures carried out daily throughout the world with contrast media.[1] Since it is also estimated that there is at least one fatality daily from the diagnostic agents,[1] principally from the water-soluble media, it is important to consider the possible protective action that might be obtained through additives to the aqueous solutions. The additives now employed vary with the source and include compounds which regulate pH, act as sequestrants, and protect against contamination. The preservatives used to protect against contamination are 0.1 per cent methylparaben (4-hydroxybenzoic acid methyl ester, USP) and 0.03 per cent propylparaben (4-hydroxybenzoic acid propyl ester, USP), and are unique to one manufacturer. These preservatives may affect the pharmacologic action of the water-soluble radiopaque media. The specific question is, then, do the parabens alter the toxicity of the media?

The toxicity of water-soluble radiopaque media is attributed by many to penetration of the blood:brain barrier. To determine the effects of the parabens on toxicity, comparative studies have been made in Rhesus monkeys* on the penetration into the brain of radioiodinated media with and without these preservatives. The media used were meglumine diatrizoate (Fig. 1)

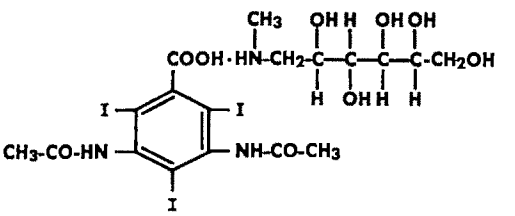


FIG. 1. Meglumine diatrizoate.

60 per cent, meglumine diatrizoate 60 per cent plus parabens, and sodium diatrizoate (Fig. 2) 50 per cent.† These media were converted to radioiodinated solutions by the addition of equal amounts of diatrizoic acid I^{125}.‡ Two 3 ml. injections of each medium were made 5 minutes apart in the carotid artery of a monkey anesthetized with pentobarbital sodium. Immediately after the injection of the second 3 ml. of contrast medium, heparin was injected and the monkey was perfused with saline. At the end of the perfusion, when the animal was dead, arterial and venous tissues were resected from the neck of the monkey, and the brain was dissected, weighed, and frozen. The tissue specimens and the whole brain were counted in a scintillation detector.§ The counting was done on all tissues at the end of the experiments so that comparisons could be made easily.

Each of the 3 radioiodinated contrast

* The Rhesus monkeys were obtained from Primate Imports, Port Washington, Long Island, New York.

† The radiopaque media and parabens are named according to USP XVII.

‡ Iodine 125 (T/2, 57.4 days; gamma-ray energy in mev., 0.0354) furnishes a label that decays slowly and can be measured by gamma-ray spectrometry.

§ The gamma-ray measurements were made in a Model 446 Armac® Scintillation Detector, Packard Instrument Company, La Grange, Illinois. Efficiency for iodine 125 was about 15 per cent.

* From the Departments of Radiology and Surgery, School of Medicine and Dentistry, University of Rochester, Rochester, New York.

This research was supported in part by grants from the Squibb Institute of Medical Research, New Brunswick, New Jersey, and from U.S. Public Health Service, National Institutes of Health, Research Grant NB 00692.

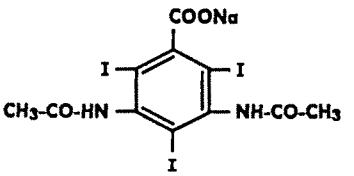


FIG. 2. Sodium diatrizoate.

media was tested in 8 Rhesus monkeys. Two perfusion techniques were employed, and 2 monkeys of each sex were used in each of the two modifications.

MATERIALS AND METHODS

The solutions of the labeled contrast media were prepared to have the composition shown in Table I. Each radioiodinated radiopaque medium was studied by two different perfusion techniques in 4 male and 4 female conditioned Rhesus monkeys. The 24 monkeys ranged in weight from 2.7 to 4.0 kg.

OPERATIVE PROCEDURE

Each monkey was anesthetized by an intraperitoneal injection of 30 mg./kg. of sodium pentobarbital. If adequate surgical anesthesia was not obtained, small additional amounts of sodium pentobarbital were administered intravenously. A longitudinal midline incision was made in the ventral neck and thorax from the level of the thyroid to the seventh costal cartilage, and the pretracheal muscles and fascia were resected to enhance exposure. A cuffed endotracheal tube was then inserted at the level of the second tracheal ring and attached to a respirator* operating with oxygen at a filling pressure of 14 mm. Hg and a respiration rate of 15–18 per minute. The clavicle and first 6 costal cartilages were severed near the junction on the left side of the sternum. Finally, the walls of the thorax were retracted laterally and held open by means of stout cord passed through the ribs on each side.

The vascular system was then prepared for the injection of the radioiodinated contrast medium and the subsequent perfusion. The tributaries of the superior vena

* Medtronic Respirator, Medtronic, 3055 Highway 8, Minneapolis, Minnesota.

TABLE I

COMPOSITION OF THE RADIOIODINATED WATER-SOLUBLE CONTRAST MEDIA*

Aliquots of diatrizoic acid I^{125} were used to prepare each of the following 3 radiopaque solutions:

Meglumine Diatrizoate 60 Per Cent		
Diatrizoic acid		472.0 mg./ml.
N-Methylglucamine		125.0 mg./ml.
Sodium citrate		3.2 mg./ml.
Ethylenediminetetraacetic acid disodium salt 3X		0.4 mg./ml.
Sodium hydroxide	q.s.	7.4 pH
Diatrizoic acid I^{125} (0.17 mg./ml.)		0.5 mc /ml.
Water for injection	q.s.	1.0 ml.
Meglumine Diatrizoate 60 Per Cent Plus Parabens		
In addition to the above identical ingredients, prepared from the same bulk, this solution contains:		
Methyl parahydroxybenzoate		1.0 mg./ml.
Propyl parahydroxybenzoate		0.3 mg./ml.
Sodium Diatrizoate 50 Per Cent		
Diatrizoic acid		483.0 mg./ml.
Edathamil calcium-disodium		0.1 mg./ml.
Sodium hydroxide	q.s.	7.4 pH
Diatrizoic acid I^{125} (0.17 mg./ml.)		0.5 mc /ml.
Water for injection	q.s.	1.0 ml.

* Each of the above 3 solutions was filled into coated 35 ml., 20 mm. vials. These were stoppered with No. H5-050 closures, and autoclaved at 15 lb. for 60 minutes.

cava were dissected free, and all branches except the two internal jugular veins were tied off. The arterial branches from the aortic arch were then dissected free, and both subclavian arteries were tied off. The objective of this procedure was to gain control over the circulation of the brain so that the internal carotid arteries remained as the sole arterial supply for the brain, while the internal jugular veins handled almost all of the venous return.

The anatomic origin of the carotid arteries was found to vary considerably so that it was not feasible to use a constant injection site. The injection was made directly into the trunk where the carotid arteries arose from the aortic arch. Where the carotid arteries had separate origins from the aortic arch, the aorta was clamped just distal to the left common carotid artery during the period of injection, and the injection made into the aortic arch. In both cases all of the radioiodinated radiopaque material was injected into the internal carotid arteries.

After the arterial system had been prepared, 3 ml. of the radioiodinated contrast medium under study was injected into the arterial blood supplying the brain over a 30 second period through a No. 25 needle. After a 5 minute wait, 3 ml. of the same radiopaque material was injected, again over precisely 30 seconds. Within 1 minute of completion of this second injection, a volume of heparin sodium sufficient to give 2,000 units per kilogram of monkey weight was administered into the arterial blood.

Following the administration of the heparin, perfusion with isotonic saline was instituted by inserting first PE 320 plastic tubing for the venous and then PE 260 tubing for the arterial catheter. The venous catheter was placed in the superior vena cava just below the junction of the two brachiocephalic veins. The arterial catheter, filled with saline and attached to the saline reservoir, was secured with a ligature into an isolated segment of the arch of the aorta adjacent to the origin of the carotid arteries. The reservoir was then raised to a height of 115 cm. above the monkey, at the level of the arterial ligature, and the perfusion of the isolated brain carried out.

Two techniques were used for the perfusion. With the first 12 monkeys, 2 male and 2 female for each of the 3 radioiodinated radiopaque media, perfusion was carried out until the perfusate was essentially free of red blood cells. Since this end point proved difficult to establish, the second group of 12 monkeys was perfused more rapidly with a uniform volume of 1,000 ml. of saline. The perfusion time was about 20 minutes with both techniques. At the end of the perfusion, the carotid arteries and the brachiocephalic and internal jugular veins were dissected, scraped clean of loose connective tissue, pressed on paper toweling, and weighed wet. The entire brain was dissected while the monkey was positioned with the head uppermost and the body dependent to prevent any blood from entering the field. The vascular samples and brain were frozen and subsequently counted for radioactivity.

MEASUREMENT OF RADIOACTIVITY

Measurements of the radioactivity of the various specimens were made in the scintillation detector. Aliquots of the radioiodinated radiopaque media, frozen whole-brain specimens, samples of the arteries and veins, and blood and perfusate samples were centered in the instrument for constant geometry of counting. Through use of the plastic support furnished for calibration of the detector, small samples of fluids or tissues contained in tubes or plastic vials were positioned in the center of the circle formed by the circumference of the chamber. The frozen brain specimens were supported at the geometric center of the tubular chamber. Contamination was avoided by enclosing each specimen in an individual plastic bag.

RESULTS

The results of the radioactivity measurements are those recorded at the end of

TABLE II

COMPARISON OF SPECIFIC ACTIVITIES OF BRAIN TISSUE FROM RHESUS MONKEYS INJECTED VIA CEREBRAL ARTERIES WITH IODINE 125 LABELED CONTRAST MEDIA AND THEN PERFUSED WITH 1 LITER OF NORMAL SALINE

Perfusion Technique	Monkey Weight (kg.)	Sex	Brain Weight (gm.)	Brain (counts per minute)	Brain Specific Activity (counts per minute/gm.)	Brain Mean Specific Activity
Meglumine Diatrizoate 60 Per Cent Plus Meglumine Diatrizoate I^{125}						
1	2.9	F	68.4	173,770	2,540	
1	2.8	F	78.2	72,989	933	
1	2.8	M	86.2	245,444	2,847	
1	3.0	M	98.9	183,650	1,857	2,045
2	3.3	F	68.7	73,159	1,065	
2	4.0	F	80.2	47,348	560	
2	3.3	M	84.6	76,527	954	
2	3.3	M	93.0	140,734	1,513	1,023
Meglumine Diatrizoate 60 Per Cent Plus Parabens Plus Meglumine Diatrizoate I^{125}						
1	3.7	F	90.4	121,742	1,347	
1	2.9	F	87.7	171,757	1,958	
1	2.8	M	91.7	129,245	1,409	
1	3.0	M	81.0	112,310	1,387	1,525
2	3.0	F	84.5	197,087	2,332	
2	3.0	F	83.0	128,252	1,545	
2	3.7	M	96.0	77,862	811	
2	2.7	M	75.3	103,964	1,381	1,517
Sodium Diatrizoate 50 Per Cent Plus Sodium Diatrizoate I^{125}						
1	2.6	F	92.1	102,105	1,109	
1	3.0	F	86.2	98,828	1,146	
1	2.9	M	81.0	99,889	1,233	
1	2.7	M	82.1	162,096	1,975	1,366
2	2.7	F	70.4	206,364	2,931	
2	2.9	F	74.6	115,506	1,548	
2	3.3	M	97.6	247,708	2,538	
2	4.0	M	83.5	124,217	1,588	2,126

all experiments when counting was done. The detector spectrometer readings were as follows: Window = 2 per cent; gain = 40; baseline discriminator = 40; and upper discriminator = 150. All samples were counted for 1 minute. The values for the radioiodinated radiopaque media in counts per minute/ml. were: meglumine diatrizoate 60 per cent plus meglumine diatrizoate I^{125}, 62,247,000; meglumine diatrizoate 60 per cent plus parabens plus meglumine diatrizoate I^{125}, 64,020,200; and sodium diatrizoate 50 per cent plus sodium diatrizoate I^{125}, 63,415,800.

Data from the studies are given in Tables II and III. The measurements of the radioactivity of the entire brain specimens from all of the monkeys are recorded in Table II. The data are grouped according to the particular radiopaque medium and are further divided into two techniques used for the perfusion. The weights of the monkeys, sex, brain weight, counted radioactivity, specific activity (SA) of the in-

TABLE III

COMPARISON OF SPECIFIC ACTIVITIES OF BRAIN TISSUE FROM GROUPS OF 8 RHESUS MONKEYS INJECTED WITH IODINE 125 LABELED CONTRAST MEDIA

Radiopaque	Specific Activity	
	Mean	Range
Meglumine Diatrizoate 60 Per Cent Plus Meglumine Diatrizoate I^{125}	1,534	560–2847
Meglumine Diatrizoate 60 Per Cent Plus Parabens Plus Meglumine Diatrizoate I^{125}	1,521	811–1958
Sodium Diatrizoate 50 Per Cent Plus Sodium Diatrizoate I^{125}	1,746	1109–2931

dividual brains, and mean brain specific activity for each contrast medium are also given in the Table. The essential data are collected in Table III to demonstrate the relationships more clearly. The measurements on the weight and radioactivity of the arterial and venous tissues removed from the monkeys are shown in Table IV.

DISCUSSION

The techniques reported here simulated clinical practice in the use of water-soluble contrast media, since two injections are frequently employed. The first injection may damage the intima so that the second injection could produce a more severe effect than the first. The measurements have been made on the effects of the contrast media only, rather than on the effect of the contrast media on the penetration of a dyestuff into the brain. Accordingly, the results have added significance for the contrast agents.

Examination of the data collected in Table II and III reveals that there was relatively little difference in the behavior of the 3 preparations investigated. Meglumine diatrizoate 60 per cent plus parabens plus meglumine diatrizoate I^{125} seems to have penetrated the brain the least of the 3 preparations, but all the values are so close that the differences are not statistically significant.

The radioactivity of the blood vessels dissected from the neck of each monkey shows interesting variations. Since the contrast media were injected directly into the blood stream through the arterial wall, it is possible that some of the radioiodinated radiopaque material may have been injected into the wall itself. This seems to have occurred with one of the injections of meglumine diatrizoate 60 per cent plus parabens plus meglumine diatrizoate I^{125}, and with two of the injections of sodium diatrizoate 50 per cent plus sodium diatrizoate I^{125}. For this reason, the radioactivity of the veins is a better measure of the comparative effect of the 3 preparations on the blood vessels. Since the recorded values show that the radioactivity of the veins was highest after meglumine diatrizoate 60 per cent plus parabens plus meglumine diatrizoate I^{125} had been injected, and the lowest after sodium diatrizoate I^{125}, this suggests that the parabens hindered the penetration of the contrast medium through the blood vessel walls. The injection of contrast media into the blood vessel wall seems to be a common occurrence, both experimentally and clinically. The original clinical observations in 1956 by Gaylis and Laws[6] on intramural injections have been extended by numerous investigators, so that Lechner[7] in his recent survey was able to tabulate data from 14 publications.

Parallel studies have been carried out by Craver *et al.*[4] in cats with the same 3 radioiodinated radiopaque media. After intracarotid injection in a manner similar to that used in the monkeys, only traces of radioactivity were absorbed by the cerebral vessels or penetrated through the blood: brain barrier. The values for the retention of the 3 media by the brain did not differ statistically. The amounts taken up were

TABLE IV

COMPARISON OF SPECIFIC ACTIVITIES OF ARTERY AND VEIN FROM RHESUS MONKEYS INJECTED VIA CEREBRAL ARTERIES WITH IODINE 125 LABELED CONTRAST MEDIA AND THEN PERFUSED WITH 1 LITER OF NORMAL SALINE

	Artery				Vein			
Sex	Weight (mg.)	Counts per Minute	Specific Activity (counts per minute/gm.)	Mean Specific Activity	Weight (mg.)	Counts per Minute	Specific Activity (counts per minute/gm.)	Mean Specific Activity
	Meglumine Diatrizoate 60 Per Cent Plus Meglumine Diatrizoate I^{125}							
F	330	49,838	151,024		200	19,328	96,638	
F	330	41,793	126,644		200	23,116	115,578	
M	350	52,917	151,191		250	25,887	103,546	
M	350	41,888	119,679	137,135	180	9,983	55,458	92,805
	Meglumine Diatrizoate 60 Per Cent Plus Parabens Plus Meglumine Diatrizoate I^{125}							
F	330	352,209	1,067,300		180	31,917	117,317	
F	260	14,283	54,935		170	14,762	86,835	
M	300	16,123	53,742		140	6,170	44,071	
M	300	25,685	85,615	315,398	180	17,151	95,283	100,877
	Sodium Diatrizoate 50 Per Cent Plus Sodium Diatrizoate I^{125}							
F	230	41,565	180,715		140	23,615	168,679	
F	400	125,172	312,930		300	19,835	66,117	
M	300	25,589	85,297		200	8,413	42,065	
M	350	32,398	92,566	167,877	200	11,085	55,425	83,071

so small that autoradiographic studies did not demonstrate significant concentrations in the brain of any radiopaque medium.

Much work has been done on the damage from water-soluble contrast media to the cerebrovascular circulation. Most of the studies have been carried out by evaluating visually the penetration of trypan blue into the rabbit brain when the dyestuff, administered after injection of the aqueous radiopaque medium, was given by a standardized procedure. This technique, as introduced by Broman and Olsson,[3] has the drawback that it gives only an indirect measurement of possible damage produced by the contrast medium or of penetration by the agent into the brain. Thus, they found that damage to the cerebral blood vessels by the contrast media of the iodopyracet group varied with the manufacturer. Obviously, the effects reported were not due to the radiopaque medium, but to extraneous impurities. Since Dobbing[5] in his review on the blood:brain barrier has pointed out the difficulties in defining the barrier in terms of a single anatomic structure for all substances, there is need for a new approach. Dobbing specifically condemns the use of dyestuffs for these studies. The radioiodinated contrast media seem to be well suited for the evaluation of their own penetration into the brain.

Additives probably can reduce the reactions from contrast media. The parabens seem to have reduced rather than increased the penetration of the radioiodinated radiopaque medium into the brain, but the effect is not statistically significant. Dextran evidently gives some protection against water-soluble media.[2] The protection that may be obtained through inert additives does not appear to be large, however, and the benefits that were initially attributed to the antihistaminics have proved disappointing.

SUMMARY

A study of the effect of parabens, preservatives used in one brand of the commercial water-soluble radiopaque media, on the penetration of the radioiodinated media into the primate brain has been carried out with Rhesus monkeys.

The radioiodinated media were prepared by adding equal amounts of diatrizoic acid I^{125} to meglumine diatrizoate 60 per cent, with and without parabens, and to sodium diatrizoate 50 per cent.

When all 3 preparations were studied under comparable conditions by intracarotid injection, the addition of the parabens may have reduced the penetration of the brain by meglumine diatrizoate slightly, but the differences were not significant.

The comparative studies were made on operated anesthetized monkeys by administering 3 ml. injections directly into the exposed carotid artery 5 minutes apart. Following the second injection, each monkey was perfused with normal saline, and the brain and other tissues removed and counted for radioactivity. All brain radioactivity measurements were determined by counting at the conclusion of the study so that direct comparison could be made.

An important incidental finding was the discovery that the blood vessels themselves retained significant amounts of the injected contrast media even after perfusion.

William H. Strain, Ph.D.
Department of Radiology
School of Medicine and Dentistry
University of Rochester
260 Crittenden Boulevard
Rochester, New York 14620

REFERENCES

1. BEELER, E. C. Wann sind Kranke bei röntgendiagnostischen Untersuchungen gefärdet? *Hippokrates*, 1960, *31*, 685–691.
2. BERNSTEIN, E. F., and EVANS, R. L. Low-molecular-weight dextran. *J.A.M.A.*, 1960, *174*, 1417–1422.
3. BROMAN, T., and OLSSON, O. Tolerance of cerebral blood vessels to contrast medium of diodrast group. *Acta radiol.*, 1948, *30*, 326–342.
4. CRAVER, B. N., CHINN, C., HESS, S. M., and SWOAP, J. B. Penetration through blood-brain barriers of cats after intracarotid injection of 125-I sodium diatrizoate, methylglucamine diatrizoate, or methylglucamine diatrizoate plus parabens and retention of 131-I methylglucamine diatrizoate in blood of rats. *Radiology*, 1968, *90*, 142–146.
5. DOBBING, J. Blood-brain barrier. *Physiol. Rev.*, 1961, *41*, 130–188.
6. GAYLIS, H., and LAWS, J. W. Dissection of aorta as complication of translumbar aortography. *Brit. M. J.*, 1956, *2*, 1141–1146.
7. LECHNER, G. Dissezierende Gefässverletzungen bei Kontrastdarstellungen der grossen Arterien. *Fortschr. a. d. Geb. d. Röntgenstrahlen u. d. Nuklearmedizin*, 1967, *106*, 596–602.

Vol. 105, No. 2

A SIMPLE BIPLANE MYELOGRAPHIC TABLE*

By H. F. W. PRIBRAM, M.D., D.M.R.D., R. E. KITCHEN, B.S.E.E.,†
and M. P. NEAL, Jr., M.D.
RICHMOND, VIRGINIA

MYELOGRAPHY, when performed properly, is a time consuming procedure. Therefore anything that helps lessen the time of the examination is valuable. A proper examination of the spinal cord includes frontal and lateral roentgenograms of the lumbosacral, lumbar, dorsal and cervical regions including the clivus in the prone position as well as a similar series in the supine position. The latter is of particular importance in lesions at the foramen magnum level, the syndrome of occult spinal dysraphism, and it may be the only way of demonstrating a spinal arachnoid cyst.

In order to obtain frontal and lateral roentgenograms rapidly and with ease, it is necessary to couple a horizontal roentgen-ray tube with a vertical one. With the mere flick of a switch one should be able to change from one tube to the other. Fluoroscopy in the lateral position is not essential, so that a horizontal beam image intensifier is not required for centering or detailed observation.

Existing units were not available for purchase in this country, nor did they satisfy our requirements. In order to reduce the cost of the project, we decided to convert a conventional 90-90 table with a motor-driven tabletop. Figure 1 shows changes made to the basic table which involved the following: (1) Removal of the counter weight from the vertical tower housing; (2) permanent mounting of the lateral tube and shutters to the vertical tower supports (A); (3) a slot was machined through the vertical tower housing for passage of the horizontal beam (B); (4) a bracket was attached to the front of the spot film device to accept "a portable lateral cassette tunnel and screen" for easy attachment and removal (C); (5) fabrication of a negator type suspension on the overhead tracks to counterbalance the combined weight of the lateral tube, spot roentgenographic device, image intensifier, and, "portable lateral cassette holder" (D); and (6) a high tension changeover switch was added to the existing 2 tube transformers for operation of the third (lateral) tube (E).

The entire unit, including spot roentgenographic device, lateral tube, lateral shutters, image intensifier and lateral cassette tunnel, moves with ease without the need for power assistance. The lateral beam follows the lateral cassette tunnel exactly and is centered above and along the table simply by moving the spot roentgenographic device. The lateral cassette can be placed close to the patient to reduce magnification. In use, we normally lock the unit in position and examine the spinal cord by operating the controls on the side of the table. The 2 controls for tilting and moving the tabletop are located at the side of the table and the whole examination can be controlled easily with 2 fingers. The patient is held with a shoulder harness.

The lateral tube is activated by a selector switch (E) and the insertion of the cassette into the lateral tunnel. This energizes the roentgenographic-fluoroscopic circuit in the control, and the exposure is made with the foot switch.

The usefulness of the table is not confined to myelography: it has also been of help in barium meal and barium enema

† Profexray Company.

* From the Department of Radiology (Neuroradiology), Medical College of Virginia, Richmond, Virginia.

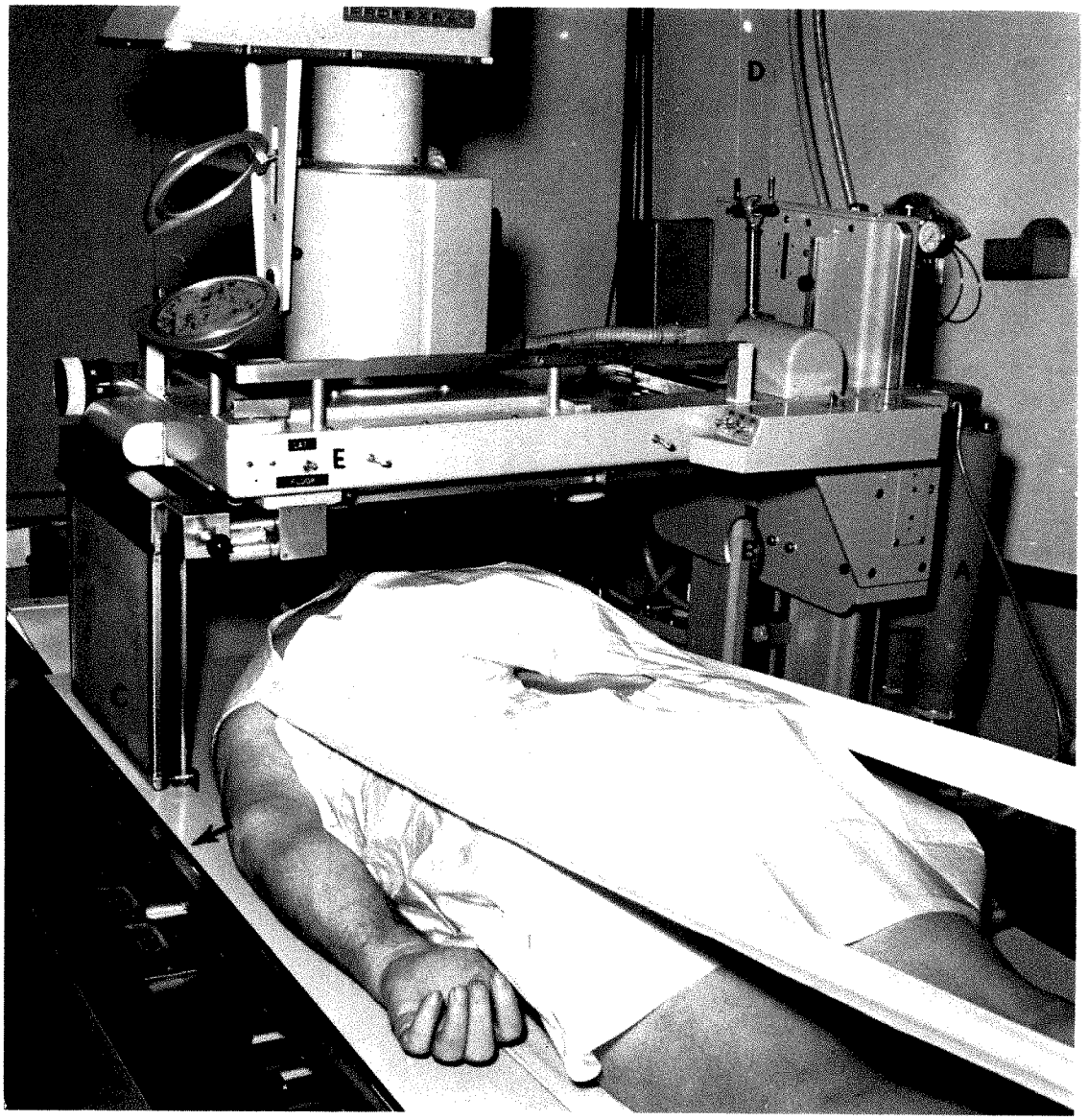


FIG. 1. Biplane myelographic table: (A) Lateral tube; (B) slot for passage of horizontal beam; (C) portable cassette tunnel and screen; (D) negator suspension; (E) selector switch to activate lateral tube; (↗) controls for tilting table and moving tabletop.

examinations. Technicians have seized on its versatility for routine roentgenographic examinations such as frontal and lateral roentgenograms of limbs in plaster.

H. F. W. Pribram, M.D.
Department of Radiology
(Neuroradiology)
Medical College of Virginia
Richmond, Virginia 23219

VOL. 105, No. 2

ULTRASONIC DIAGNOSIS OF SUBDURAL HEMATOMAS*

By JEFFREY ROTHMAN, M.D., STANLEY SHATSKY, B.S., IRVIN KRICHEFF, M.D., *and* NORMAN CHASE, M.D.
NEW YORK, NEW YORK

A SIMPLE, quick and quantitative method of diagnosing subdural hematomas in the critically ill patient is needed to screen such patients for possible cerebral angiography. Ultrasonic diagnostic techniques offer such an approach. We have employed a focused transducer for near side visualization of the subdural hematoma, using the space averaging technique of Ford and Ambrose[5] and McKinney.

Early efforts in the ultrasound diagnosis of brain lesions were limited to detecting shifts in the midline echo.[4] Subdural hematomas cause a shift with several exceptions.[5,10,11] There is frequently no shift if the subdural hematoma is bilateral, if the hematoma is small or if there is cerebral atrophy on the same side as a chronic subdural hematoma.[11] A cerebral contusion without a subdural hematoma may also cause a shift of the midline structures.

Echoes have often been difficult to obtain on the side of a subdural hematoma. Ford and Ambrose[5] found that in 13 out of 23 patients with subdural hematomas there was a decreased amplitude to the midline echoes or absence of the midline echo. This was more pronounced at sound energies of 2.5 megacycles than 1.5 megacycles. Lithander[10] noted that with an intracerebral expanding mass (in contrast to an extracerebral mass) the midline echo varied with the placement of the transducer.[10]

Initial attempts to diagnose subdural hematomas were strikingly unsuccessful with placement of the transducer on the side of the lesion (near side). The "main bang" or artifact from the machine itself fell in the area under study and also there was lack of resolution in this area. Therefore, early efforts were confined to placement of the transducer on the side opposite the subdural hematoma (the far side). When the A mode of ultrasound[4] was used to visualize subdural hematomas on the far side, the hematoma would frequently give an echo or echoes before the echo from the adjacent inner table of the skull.[2,5,7,9,18–19] Mainly utilizing the far side echoes several investigators came to the following conclusions: Ter Braak *et al.*[15] felt that the plane separating the hematoma from the brain sometimes gave a detectable echo with no specific features. Ambrose[2] believed that often in subacute and chronic subdural hematomas (but only occasionally in acute hematomas) there was an abnormally placed echo deep to the inner table due to the interface produced by compression of the subarachnoid space and underlying brain. De Vlieger observed a single echo or a complex of echoes. He thought that in a chronic subdural hematoma a complex is seen due to inhomogeneities caused by clots. Ambrose[2] reported that diagnosis of subdural hematoma was easy in the fronto-temporo-parietal area; however, subdural echoes were undetected in other transducer positions and only a midline shift was seen. De Vlieger had better results diagnosing acute subdural hematomas than chronic subdural hematomas.

A special transducer position was used by De Vlieger.[6] He placed it on the mastoid and angled it upward to have the sound waves cross the bulk of the hematoma, which was usually parietal. This also made the beam more perpendicular to the hematoma-brain interface. To get the beam even more perpendicular, he used a perspex block so that the beam struck the skull at

* From the Department of Radiology, New York University School of Medicine, New York, New York.
Supported in part by Training Grant NB5433 and ES00116.

a 45° angle. Besides detecting extra echoes, the amplitude of the final skull echo complex was decreased.

Jeppson[8] and Lithander[11] objected to all the methods so far discussed because the echoes from the supposed subdural hematoma could not be differentiated from "impressiones digitatae, broad gyrus or fissure echoes." To overcome this objection De Vlieger utilized a moving probe technique to determine if the echo was caused by a planar surface.

Differing results have been reported for methods using the far side echo criterion. Wagai *et al.*[18] diagnosed 22 out of 25 extracerebral hematomas correctly. Tanaka and Wagai[14] diagnosed 15 out of 16 and added that they could also diagnose the extent and depth of the hematoma. De Vlieger had poor results, diagnosing only 15 out of 43 subdural hematomas.

The disadvantages of far side studies using the probe on the mastoid are greater absorption in travelling a longer distance, the greater effect of variations in angulation of the beam at a greater distance, and scattering of the beam when striking a convex surface. These problems led De Vlieger to attempt to obtain abnormal hematoma echoes on the side immediately underneath the probe. Using a combination sender-receiver transducer, reflecting surfaces situated close to the probe could not be detected since the echoes returned to the probe during the period when the amplifier was blocked by the transmitting pulse. Therefore, De Vlieger used a separate sender and receiver. A hematoma was diagnosed if echoes were seen that were not present on the normal side. A frequent large echo complex from the skull, however, made interpretation difficult. He concluded after producing an artificial hematoma at autopsy that there was no simple picture due to one definite echo from the subdural hematoma and that the echogram only demonstrated a collection of fluid outside the brain.

Recently attempts have been made to diagnose subdural hematomas using the B or cross-sectional mode of ultrasound.[4] Adapon *et al.*[1] missed all the subdural hematomas except one. In this one case the subdural hematoma was seen displacing the brain on the far or contralateral side. Galicich *et al.*[6] diagnosed 2 out of 8 subdural hematomas in infants by the B scan on the near side. Both of these were unilateral subdural hematomas at least 1 cm. in thickness in some areas. A possible explanation for the lack of success was that the pulse artifact or "main bang" from the machine and the multiple echoes from the skin and bone caused a decrease in resolution in the vicinity of the subdural space.

METHODS AND MATERIALS

The equipment used in our work was the Hoffrel 101 b ultrasonoscope. The 703 E.K.G. slow sweep control box was also used. A focused 2 megacycle sound transducer having a 3 cm. focal distance was employed. All studies were done in the B mode. In this mode an echo at an interface between tissues of different acoustic impedance (density times velocity) appears as a dot. The greater the impedance mismatch at the interface the greater the amount of energy reflected giving a brighter (more intense) echo. The patients are examined at 5 positions on each side of the head. These positions were located by drawing a line (mv) perpendicular to the canthomeatal line (cm) at the external auditory meatus. Three points were located at 4 cm., 6 cm., and 8 cm. above the meatus on this line. Lines cm^{I} and cm^{II} were drawn parallel to line cm, 6 cm. and 8 cm. above it. The fourth point was located on cm^{I} 2 cm. (usually) or 3 cm. anterior to line mv. The fifth point was placed on line cm^{II} 4 cm. posterior to line mv. When the point on line cm^{I} was placed 3 cm. anterior to mv it was very difficult to obtain good pictures. Examination at 5 points on the head is critical since a subdural hematoma may be present only in small loculated areas corresponding to only 1 of the 5 positions. The area to be examined was swabbed with glycerine or aquasonic 100

ultrasound gel and the hair was pushed aside. When the hair was very thick, long and curly or the opposite side of the head was shaved, the area under examination was also shaved. The transducer was firmly applied to the head and the marker or linear calibration scale on the cathode ray tube was expanded to 7 cm. for easy visualization. Care was taken to keep good contract and not to allow the transducer to slip down and anteriorly in the lower positions because this could cause false positives. Echoes appeared as a line of dots at the bottom of the screen indicating reflecting interfaces at different depths. The space averaging technique of Ford and Ambrose[5] and of McKinney was used in which the transducer was rocked at a 5 degree angle in a coronal plane. A rocking motion was used since initial experiments without any motion produced pictures inadequate in detail. They lacked any fine structure and the echoes were too closely packed; also without any motion the artifacts of pressure used were too numerous. A coronal rather than a conical rocking motion also eliminated much artifact. When this method is used the strongest echoes remain and the weaker ones disappear. No unique search and find procedure is used. The presence and position of the echo is the most important criterion. A large contrast adjustment is required in adults in order to eliminate weak unimportant echoes.[11] The strong significant echoes remain. The transducer is placed flat against the head. If any series of echoes are present on the cathode ray tube, the foot pedal is depressed and the coronal rocking motion is initiated. No attempt is made to pick out the "best possible" echo patterns. Therefore the procedure is more objective due to this "blind" technique. The result of sweeping the dots across the screen (at a sweep period of 8 seconds) are continuous or interrupted lines, which represent sound reflecting interfaces. The echoes are photographically recorded as seen in Figure 1, *A* and *B*. Usually a few sets of pictures are reproducible. Consistency of echo pattern is necessary for any study. The settings for the machine are shown in Table 1.

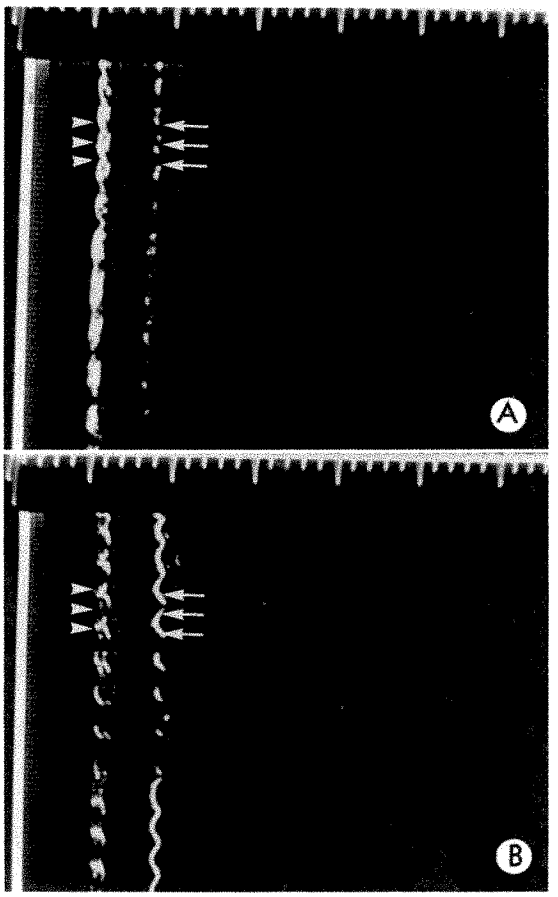


FIG. 1. (*A* and *B*) This is a normal 2:2 pattern. Line 1 (arrowheads) represents the inner table-cerebrospinal fluid meningo-brain interface. This depth is constant (0.9–1.1 mm.). Line 2 (arrows) represents the gray-white matter interface.

Sixty hospital patients between 6 months and 83 years of age were examined. Thirty-three were head trauma patients suspected of having a subdural hematoma. Twenty of these patients were diagnosed by angiography or surgery. Ultrasound examination was done on 6 of the positive 12 patients with previous knowledge of the diagnosis of subdural hematoma; however, for the most part the side was unknown to us. Only one false side localization of a subdural hematoma was made. This will be discussed in detail later. Two patients with intracerebral hematomas and

TABLE I

SETTINGS FOR ADULTS
(S more frequently used)

	(S)	(T)
Contrast	11 (maximal)	11
Pulse pressure	3	3
Clipping	4	4
Damping	4	2
Fine gain	7·5	7·5
Coarse gain	4.8	7.2
Range	0–7	0–7
Sensitivity		
Depth Control	½–6	½–6

For babies contrast in S and T is set at 0.
The brightness is always set at a point just below that at which a horizontal line disappears from the cathode ray tube.

1 with a tumor were also studied. Twenty-four neurologically normal patients from the medical service were used as controls. Four subdural hematoma patients were followed over an extended period of time.

RESULTS AND DISCUSSION

The normal pattern consists of 2 or 3 echoes seen as lines on each side of the head (Fig. 1, *A* and *B*). The first echo falls between 0.9 and 1.1 cm., is usually 0.3 to 0.4 cm. wide and shows a 4+ brightness on a 4+ scale. We feel that this represents reflected sound from the inner table-meningo cerebrospinal fluid-brain interface complex, because there is a great echo producing acoustic impedance mismatch at the interface between the cerebrospinal fluid and the bony inner table with adherent dura. This echo producing interface has been described on the near and contralateral side by Elizondo-Martel and Gershon-Cohen[4] and others.[2,5,7,9,13–19] Elizondo-Martel described 2 separate echoes caused by the inner table and the brain meninges complex which are 3–4 mm. apart, corresponding to the width of the cerebrospinal fluid layer. We have sometimes noted a similar double echo in subdural hematoma patients 2 mm. apart with different setup settings. Furthermore on the normal side (Fig. 2) we have occasionally been able to see the first echo split into 3 lines. However, the majority of times it is a single thin strong echo or is a strong echo 3 to 4 mm. wide. In Figure 2 we see the first and third echoes 3 mm. apart corresponding to the anatomic distance between the inner table and the brain itself. The 3 lines are felt to represent 3 interfaces as would be expected since there are 3 interfaces where there would be an impedance mismatch. They are: the inner table-dura interface, the dura-cerebrospinal fluid interface and the cerebrospinal fluid-brain interface. We feel that the cerebrospinal fluid-brain interface contributes to this echo complex since it has been proved that sounds are reflected from the ventricular cerebrospinal fluid-brain interface.

Evidence for the origin of echoes from gray-white matter interfaces as well as cerebrospinal fluid-brain interfaces comes from the work of Lithander[12] and Dreese and Netsky[3] who worked on autopsy specimens. Lithander[12] stated that echoes originated from gray-white matter interfaces of the thalamus, internal capsule, and external capsule as well as from brain-cerebrospinal fluid interfaces of the ventricles and gyri.

Dreese and Netsky[3] stated that reflections arose predominantly from interfaces of brain and cerebrospinal fluid and with

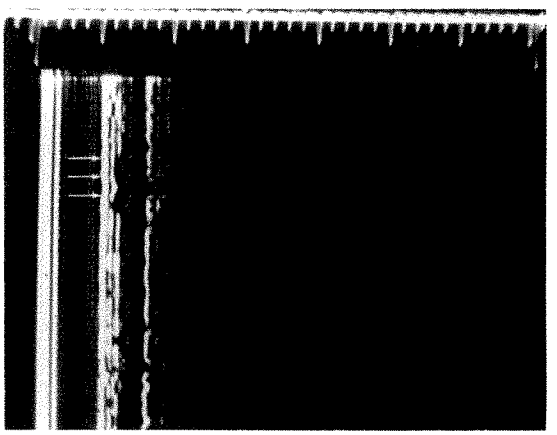


FIG. 2. This is a normal side. The first echo is split into 3 separate lines representing the inner table-dura interface, the dura-cerebrospinal fluid interface and the brain-cerebrospinal fluid interface.

slightly less amplitude from interfaces between white and gray matter such as the *insular cortex*, claustrum, basal ganglion (putamen and pallidum as well as thalamic internal capsule junction).

The second echo producing interface is between 0.4 and 1.2 cm. deeper. This area between the 2 echoes may rarely be filled by horizontal echoes (Fig. 3, *A* and *B*). We have noted this to be a function of the machine sensitivity controls. The location is consistent with the distance from the surface of the brain to the gray-white matter interface, which has been shown to be a sound reflecting interface. For unexplained reasons this has been seen as a double echo in only subdural hematoma patients (on the abnormal side in 1, and bilaterally in 2). The strength of the echo is 4+ and it may or may not be as wide as the brain-cerebrospinal fluid complex.

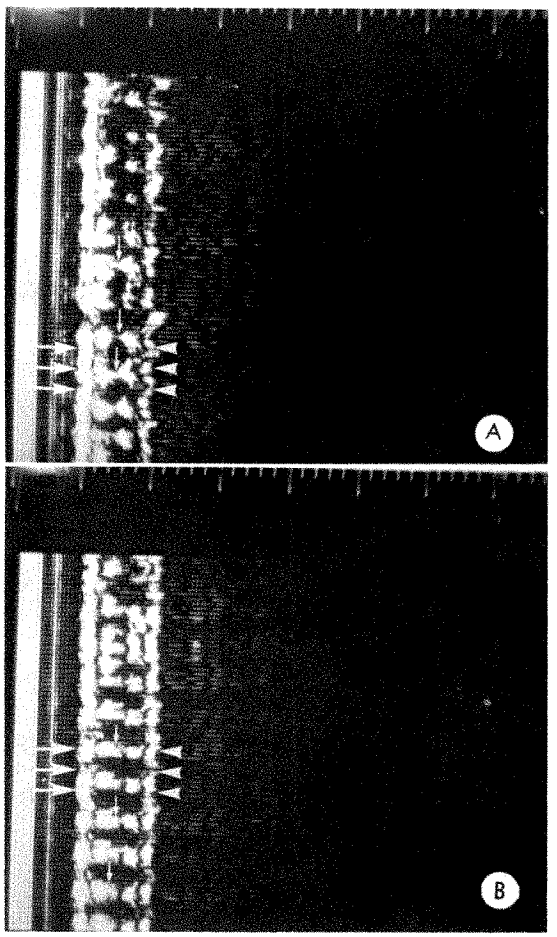


FIG. 3. (*A* and *B*) Normal 2:2 pattern with horizontal "fill-in." Line 1 (large arrows) represents the inner table-cerebrospinal fluid brain complex; the small white arrows point to the variant fill-in pattern between the 2 lines. The arrowheads show the gray-white matter interface.

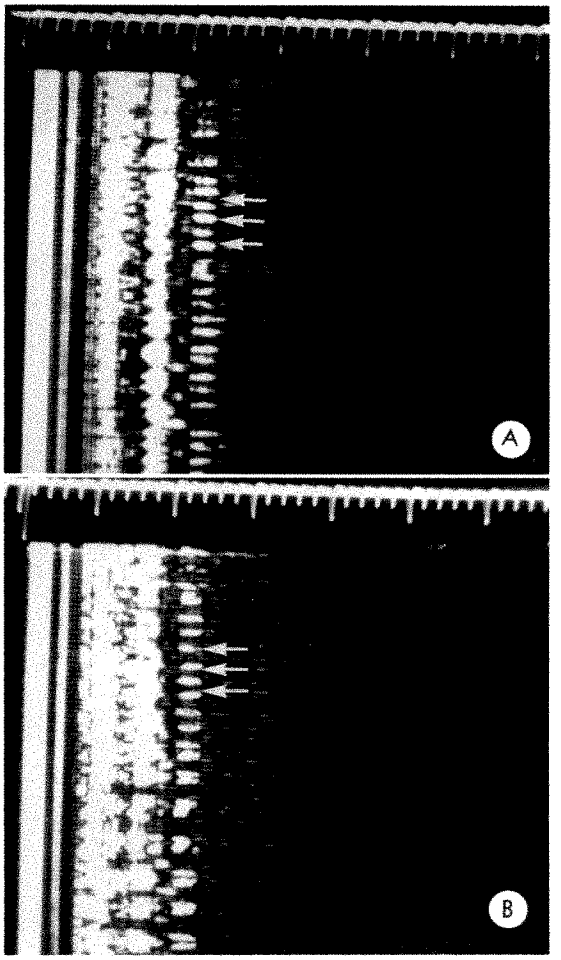


FIG. 4. (*A* and *B*) Normal 3:3 pattern. Arrows indicate periodically interrupted 3rd line representing the insula. Some patients have shown solid symmetric 3rd echoes.

The third echo is seen only when the probe is over the insula (Fig. 4, *A* and *B*). Here another brain-cerebrospinal fluid echo producing interface is seen. This area is the only one where a bilaterally *symmetric* third echo is considered normal. This is sometimes seen on the 4 cm. position on the line perpendicular to the canthomeatal line and less constantly on the 6 cm. position. We believe that this normal third

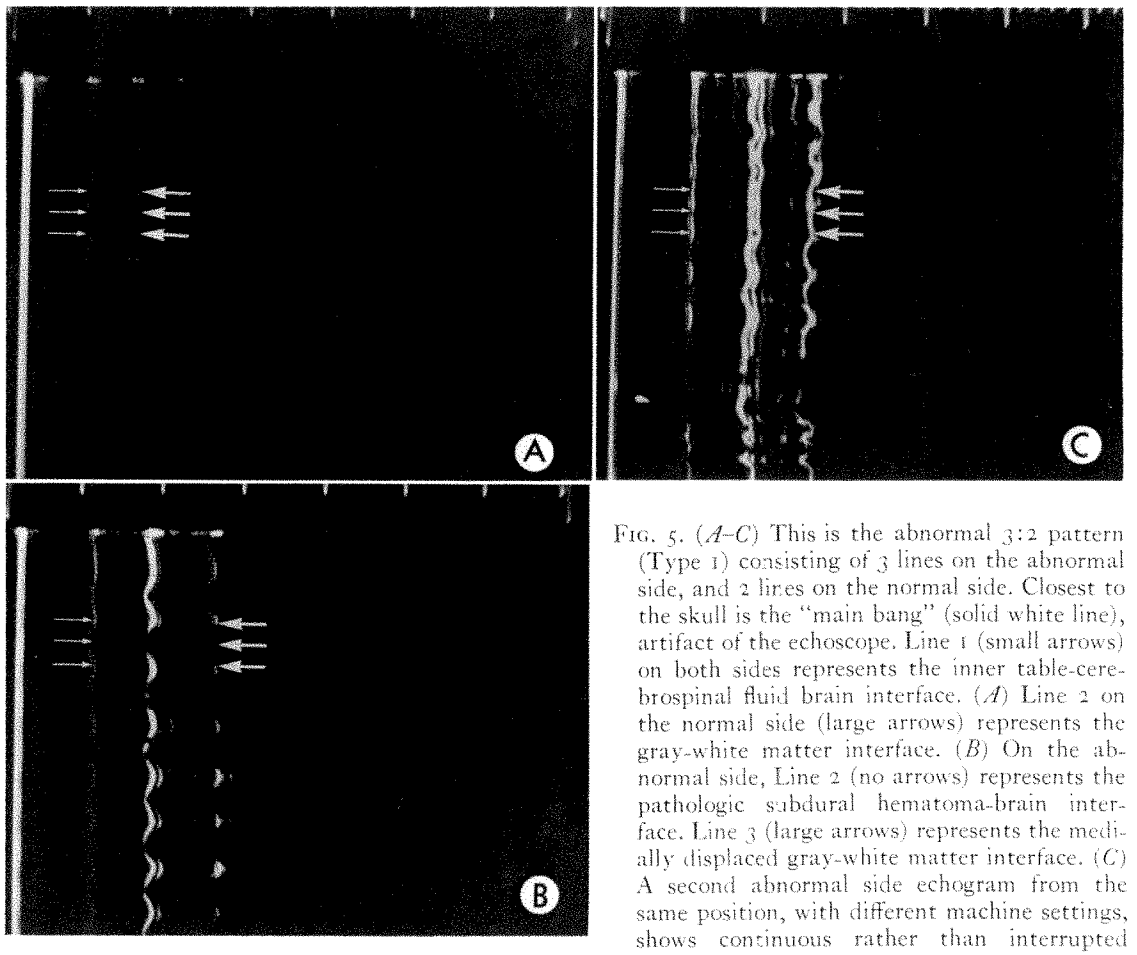


FIG. 5. (*A–C*) This is the abnormal 3:2 pattern (Type 1) consisting of 3 lines on the abnormal side, and 2 lines on the normal side. Closest to the skull is the "main bang" (solid white line), artifact of the echoscope. Line 1 (small arrows) on both sides represents the inner table-cerebrospinal fluid brain interface. (*A*) Line 2 on the normal side (large arrows) represents the gray-white matter interface. (*B*) On the abnormal side, Line 2 (no arrows) represents the pathologic subdural hematoma-brain interface. Line 3 (large arrows) represents the medially displaced gray-white matter interface. (*C*) A second abnormal side echogram from the same position, with different machine settings, shows continuous rather than interrupted echoes. Arrow markings are as above.

echo is produced because the insular echo beam angle is more perpendicular than other parts of the brain. At this distance from the focal point of the transducer only the cerebrospinal fluid-brain interface can be seen since it has a larger impedance mismatch than the gray-white matter interface[3] which moreover is farther from the focal point.

There are 2 distinct subdural patterns. Pattern 1 shows a reproducible third echo due to a new sound reflecting interface located between the altered brain-cerebrospinal fluid complex and the gray-white matter interface (Fig. 5, *A–C*). This new middle echo may be localized or widespread corresponding to the extent of the subdural hematoma. The distance between the pathologic echo and the gray-white matter interface is consistent with the thickness of the gray matter, leading us to agree with Ter Braak *et al.*[15] and Ambrose[2] that this line represents the hematoma pressing upon the brain. Type 1 consists of the normal 2 echoes on the one side and 3 echoes on the pathologic side. The middle of these 3 echoes represents the subdural hematoma pressing on the brain. The surrounding echoes are first the normal brain-cerebrospinal fluid interface and then the outer echo representing the gray-white matter interface.

In a variant of Type 1 found in most of the pictures of 2 to 12 patients correctly diagnosed as to presence and side of subdural hematoma, the space between the echo from the altered brain-cerebrospinal fluid complex and the hematoma-brain

interface—corresponding to the hematoma itself—is filled in by horizontal echoes (Fig. 6). This pattern is thus a variation of the 3:2 Pattern, 1′; it is felt to be a machine made pattern, however, having a significance the same as a simple Pattern 1, since when the contrast is one half of normal it is seen that these extra echoes appear (Fig. 7, *A* and *B*). This is also dependent on the thickness of the skull, the age of the patient, the setting of the "compensating" sensitivity depth control and the settings of the damping control. If contrast is less (*e.g.*, approximately below 6 on our machine for an "average patient") the echoes are thicker and deeper and the pattern is obscured.

Pattern 2 (Fig. 8, *A–C*) found in 5 of 12 subdural patients did not show a second and third line which could be identified. There were, instead, multiple or massed vertically parallel compression lines of equal strength in the region corresponding in general to the area between Lines 2 and 3 in the previous subdural hematoma types. There is no strong Line 3 as in the other patterns. (A definite gray-white matter interface could only be determined experimentally by probing with the tip of a needle.) We believe this area of vertical

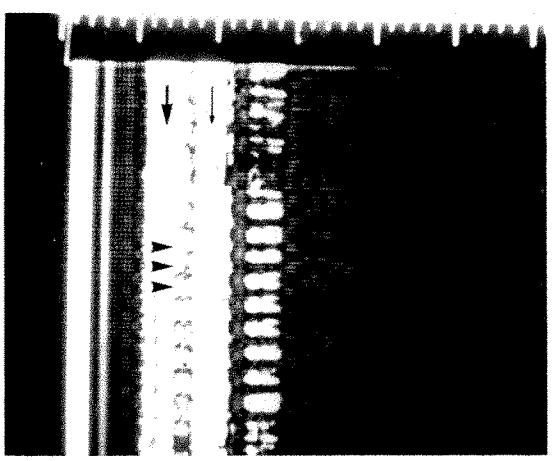


Fig. 6. Subdural hematoma variant of Type 1 pattern. A 3 line pattern is seen with a horizontal "fill-in" (arrowheads) between Lines 1 (large arrow) and Line 2 (small arrow). The fill-in pattern empirically correlated with a hematoma of 1 cm. or greater size.

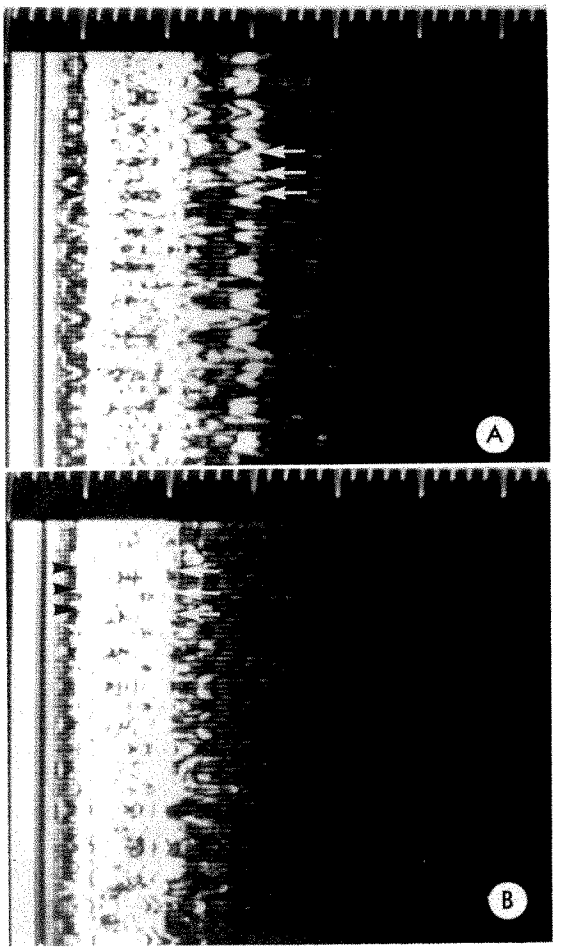


Fig. 7. (*A* and *B*) This is a variant of Type 1 pattern with decreased contrast. (*A*) The abnormal side again shows the 3 line pattern, with 2 lines on the normal side *B*. Horizontal filling is seen on both the normal and abnormal sides—a result of the decreased contrast. Black arrowheads show the inner table-cerebrospinal fluid brain interface, white arrows the gray-white matter interface.

echoes to represent the area of compressed brain possibly with a contribution of the hematoma itself. One picture (Fig. 9) suggests that the vertical echoes of the Type II pattern fall between the subdural hematoma-brain interface and the gray-white matter interface. This picture has definite intense first, second and third echoes with less intense vertical echoes between. The area between Lines 2 and 3 in this picture corresponds exactly to the area of vertical echoes of the Type II pattern. This implies that the vertical echoes of this Type II

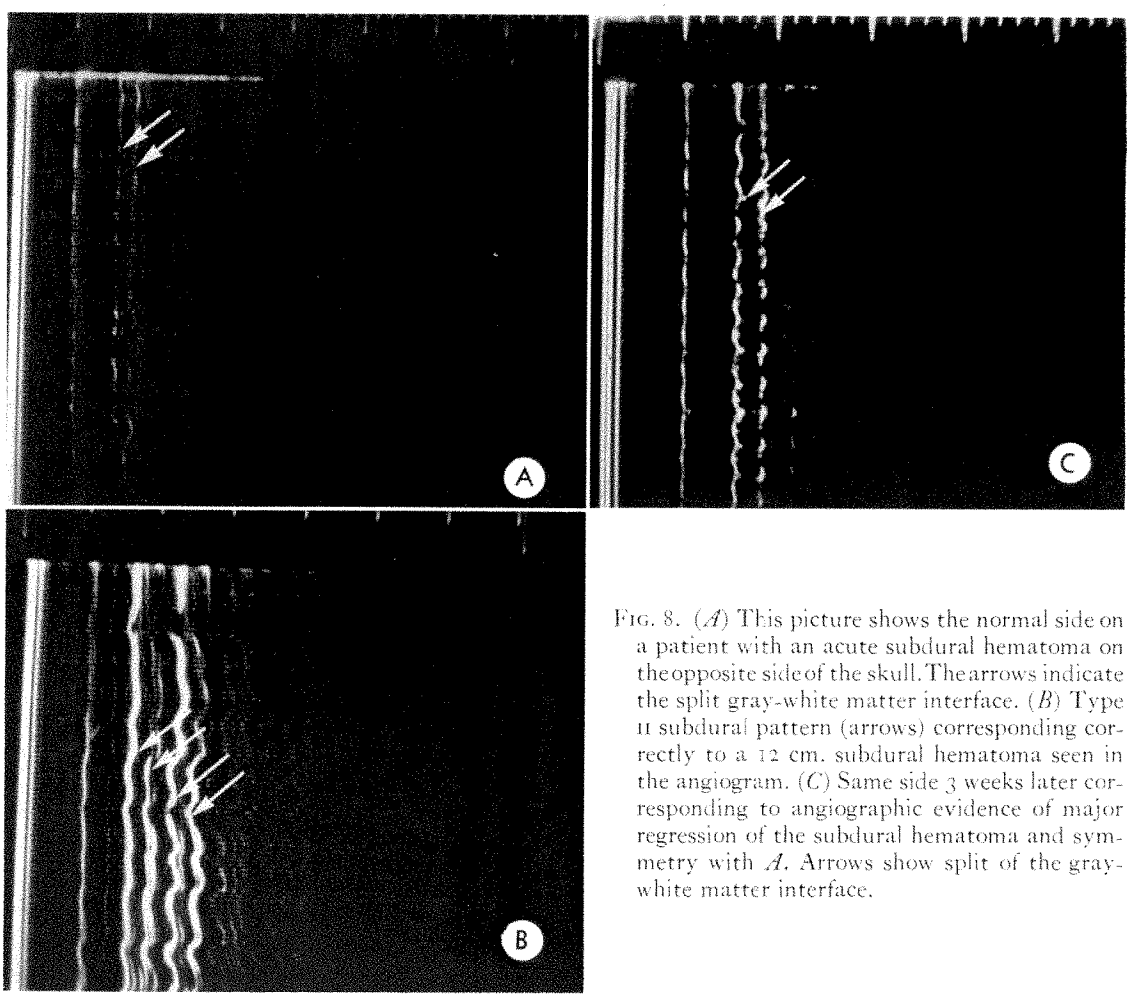


FIG. 8. (*A*) This picture shows the normal side on a patient with an acute subdural hematoma on the opposite side of the skull. The arrows indicate the split gray-white matter interface. (*B*) Type II subdural pattern (arrows) corresponding correctly to a 12 cm. subdural hematoma seen in the angiogram. (*C*) Same side 3 weeks later corresponding to angiographic evidence of major regression of the subdural hematoma and symmetry with *A*. Arrows show split of the gray-white matter interface.

pattern are caused only by lines of compression between the subdural hematoma-brain interface and the gray-white matter interface. The width of this area, as will be stated later, was useful in estimating the size of the subdural hematoma. The attractive hypothesis that the lines represented anoxic compression of brain by an acute subdural hematoma was not borne out in this study. Further evidence of the abnormality of the third line and its causation by the pressure of the hematoma was found in 2 patients. In a baby 6 months old immediate post-tap (38 and 12 cc.) echograms on 2 occasions showed the disappearance of the third line with the appearance for the first time of deeper echoes (Fig. 10, *A–D*). In one patient 30 years old, repeated examinations showed decrease in the size of the subdural hematoma with ultimate disappearance of the third line (Fig. 8, *A–C*).

Since we only saw 1 bilateral subdural hematoma, we cannot say for certain whether a bilateral 3 echo pattern (which must be asymmetric over the insula) will consistently be found; however, all other evidence points to this conclusion. In spite of this, the presence of "the third line" was our major criterion in making the diagnosis of a subdural hematoma.

A discussion is warranted at this point of our 1 bilateral subdural hematoma patient. Initially, we knew that he had a subdural hematoma by asymmetry as considered immediately below; however, we did not know if the subdural hematoma was

bilateral or how large it was, since it was at the beginning of our study and our methods were not perfected. We knew that it was bilateral only from the angiogram. After the angiography the patient was tapped bilaterally. The reaccumulation of fluid was known to be bilateral since both sides showed an outward movement of the final lines on echo examination. This was confirmed at autopsy which showed a bilateral hygroma.

A second important criterion for diagnosis of a subdural hematoma is an asymmetry greater than 3 mm. between the final echoes (Line 2 on the normal side and Line 3 on the subdural hematoma side) representing the gray-white matter interfaces.

An additional less important criterion is that a "midline echo series" beyond the gray-white matter interface is present when the transducer is placed on the normal side, but not when it is placed on the side of the subdural hematoma. In the 6 month old baby these midline echoes appeared immediately after the tap, not having been visualized from the side of the lesion before. Also the brain was seen to move toward the side of the tap.

There are 2 additional criteria involving the technique to double check the abnormal results so that artifact may be ruled out. If the pattern persists in 2 or more positions and multiple subdural patterns are seen, artifacts may be ruled out.

Two patients with intracerebral hematomas (Category D, Table II) were seen. One exhibited a normal 2:2 pattern. The other patient whose hematoma was believed to be frontal clinically showed a 3:2 pattern. The asymmetry between the final echoes was less than 3 mm. or within normal limits excluding the diagnosis of a subdural hematoma (Fig. 11, *A* and *B*).

The patient with a tumor on the right side also exhibited a 3:2 pattern which was quite different from the subdural hematoma pattern. Bilaterally there were echoes between 0 and 1.1 cm. and 1 at 1.5 cm. However, the third echo at 2 cm. was very dim, interrupted and was very thin. Moreover, the third echo was on the left side, contralateral to the tumor. Possibly visualization of the insula occurred due to pressure by the tumor. A midline shift would be expected. The one subdural hematoma that was missed was the largest in our series; it showed a prominent bright second echo on the side opposite the hematoma and no gray-white matter interface echo on the side of the lesion.

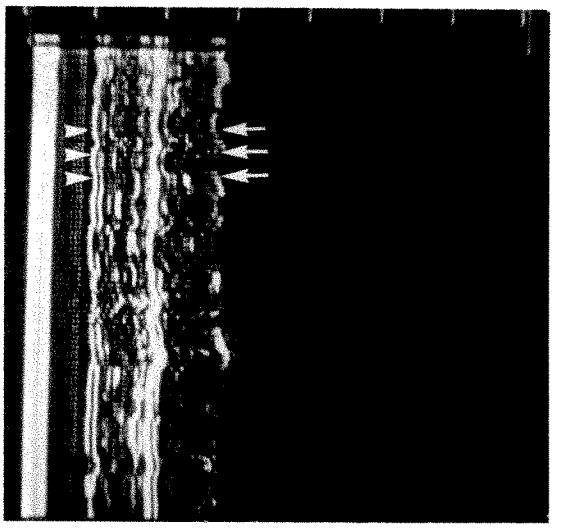


FIG. 9. This is a variant of the preceding 3:2 pattern (Type I) with vertical echoes filling the area between Line 1 (white arrowheads) and Line 3 (white arrows) on the abnormal side. Such patterns with vertical fill-in echoes between the main echoes indicate subdural hematomas of 1 cm. or greater diameter. The subdural hematoma in this patient was 12 mm. measured angiographically. A Type II pattern in this patient filled in the area exactly between Line 2 (no arrows) and Line 3 (white arrows).

Artifacts must be differentiated from true patterns. Artifacts usually are caused by insufficient transducer coupling in which the upper edge and, less frequently, the lower edge of the transducer lose contact with the skin. These artifacts are produced most easily 4 cm. anterior to the 6 cm. point on Line mv. These reverberations or "ghosts" are caused by reflections between the skull or skin and the transducer. Anteriorly, the large diploic spaces in the frontal bone are believed to be the source

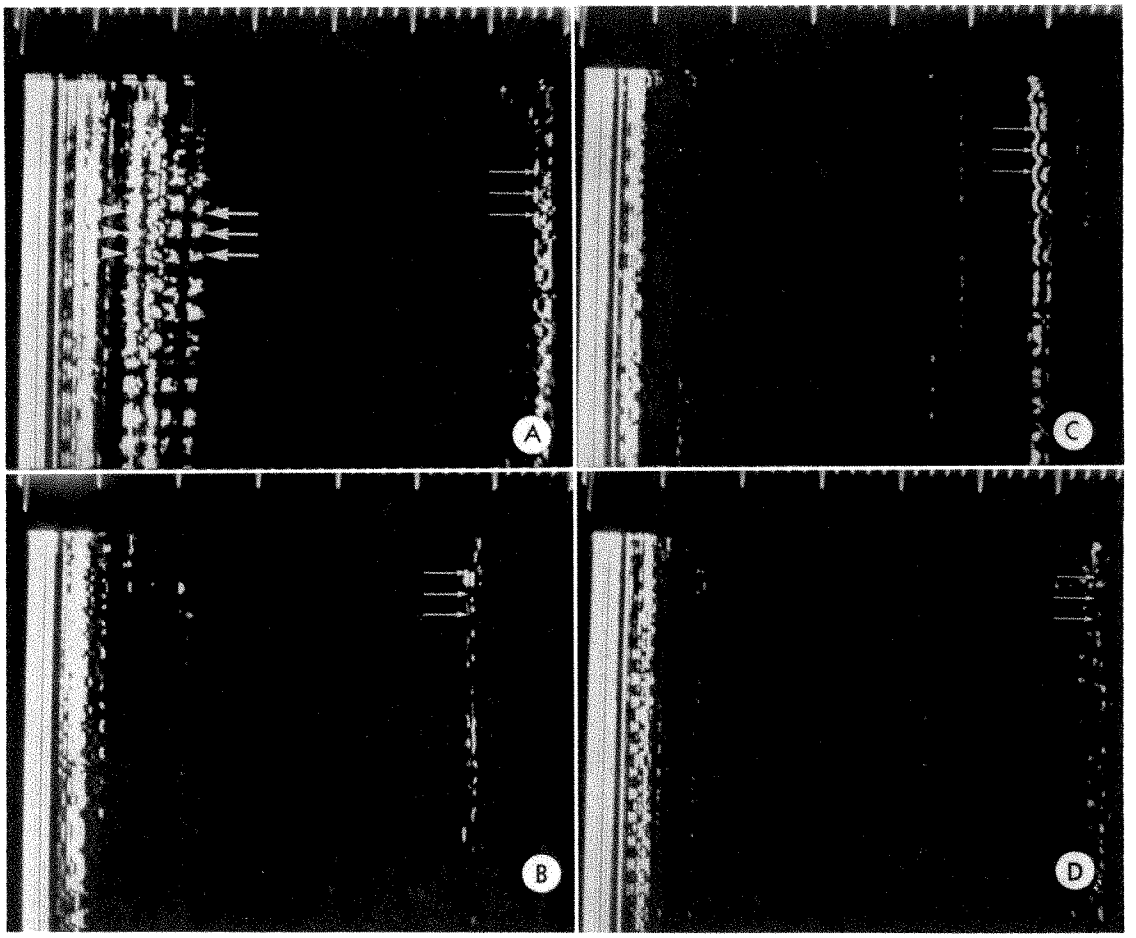


FIG. 10. (*A*) Type II subdural pattern in a 6 month old baby with vertical "fill-in" echoes in the same general area where echoes 2 and 3 would be expected in other hematoma patients. (*B*) Normal side of the patient. (*C*) Abnormal side, 3 hours after tapping 38 cc. of blood. The echoes of Type II pattern have disappeared. (*D*) Normal side, 3 hours after the tap. The "midline echoes" (small arrows) are shown to shift past the anatomic midline toward the abnormal side with tapping.

of excess reverberations. They consist of between 3 and 6 dense white lines (0.1 to 0.6 cm. wide) which may be spaced equidistantly at from 0.7 to 0.9 cm. (Fig. 12) or may be separated by alternating distances of 10 and 6 cm. (Fig. 13). The width and intensity of these lines will decrease at greater depths. The deepest echoes may be seen at approximately 4.5 cm. in adults with normal skull thickness. Another artifactual pattern of 4 equidistant (0.9 cm.) very strong lines (with no other echoes on the screen) will often appear or disappear together as a group. This 4 line artifact pattern is more commonly seen in abnormals. A 3 line reverberation pattern is more frequent in normals.

In addition to supplying the second diagnostic criterion, asymmetry gave a guide to the size of the subdural hematoma. This quantitation of the subdural hematoma was done by measuring the asymmetry betwen Line 2 on the normal side and the outermost line on the side of the lesion—both being echoes at the gray-white matter interface. Measurements between Lines 1 and 2 and Lines 1 and 3 on the abnormal side show the former to be constant (not changing with subdural hematoma size) between 0.6 and 1.0 cm.

TABLE II

SUMMARY OF THE CLINICAL RESULTS

Types of Patients Studied	Echo Finding	Confirmatory Study	Comment
A 12 trauma patients who subsequently were found to have subdural hematomas; 11 had unilateral and 1 had bilateral subdural hematomas	a. 11 subdural hematomas diagnosed as to side and size b. 1 abnormal pattern	9 positive for subdural hematoma by angiography, 1 by surgery, 1 by repeated taps, and 1 by angiography plus autopsy	b. the abnormal echo pattern was different from the normal or subdural patterns; 1 patient had unilateral subdural hematoma and bilateral dilated ventricles (demonstrated by angiography) which did not obscure the diagnostic pattern
B 21 trauma patients who subsequently were found not to have subdural hematomas B_1 8 confirmed by contrast examination B_2 13 confirmed by clinical examination	B_1 a. 7 no subdural or abnormal pattern b. 1 bilateral subdural pattern B_2 a. 11 no subdural pattern, normal echo pattern b. 2 normal, but variant echo pattern	B_1 a. 7 negative for subdural hematoma by angiography b. angiography and pneumoencephalography negative for subdural hematoma but positive for bilateral dilated ventricles B_2 clinical course negative for subdural hematoma	B_1 b. bilateral dilated ventricles reproduced the bilateral subdural pattern B_2 b. non-variant pattern (see text)
C 24 neurologically normal patients used as controls	a. 23 no subdural or abnormal pattern b. 1 bilateral subdural pattern	a. clinical course negative for subdural hematoma	b. bilateral dilated ventricles produced the subdural pattern
D 3 patients known to have intracerebral mass lesions (2 intracerebral hematomas, 1 neoplasm)	D_1 a. 2 intracerebral hematomas, 1 no subdural or abnormal pattern, and 1 unilateral subdural pattern by criterion 1 D_2 a. 1 tumor, no subdural but an abnormal pattern	clinical course negative for subdural hematoma angiography negative for subdural hematoma	D_1 the pattern or criterion 1 was satisfied; however, the asymmetry between the final echoes was within normal limits (criterion 2) D_2 the pattern was evidently different from the subdural pattern

and the latter constant between 4 and 1.4 cm., whereas the asymmetry between Lines 2 and 3 had a range between 5 and 15 cm. as seen in Table III. The quantitation was reliable to 1 cm. on the angiogram. The asymmetry method was more sensitive than the midline or A scan on echogram and/or shift of the internal cerebral vein on the angiogram, since a significant number of small subdural hematomas less than 1 cm. did not show a shift of greater than 0.3 cm. in these echographic and angiographic studies, especially if contralateral cerebral edema was present. In 5 cases out of 10 (including the 1 bilateral subdural hematoma case) the asymmetry criterion for size agreed with the angiographic measurement of size to within 2 mm. In 4 cases, excluding the subdural hematoma which was misdiagnosed as to side, there were masses of echoes between Lines 1 and 2 (Type 1′), the general area between Lines 2 and 3 (Type 11), or Lines 1 and 3 (a combination). The finding of this "fill-in" pattern was correlated well with the findings of a large subdural hematoma greater than 1 cm. The width of the vertical echo band in the "general area" between Lines 2 and 3 with no accompanying band between Lines 1 and 2 correlated well with the size of the subdural hematoma. The band ranged between 10 and 17 mm. However, the width of the band between Lines 1 and 2 did not correlate with the size as well as the asymmetry between the final lines, *i.e.*, between Lines 2 and 3.

Table 11 summarizes the clinical results of this study. Sixty hospitalized patients were studied for subdural hematoma. Thirty-three of these patients were admitted for head trauma. Twenty-four were neurologically negative medical patients

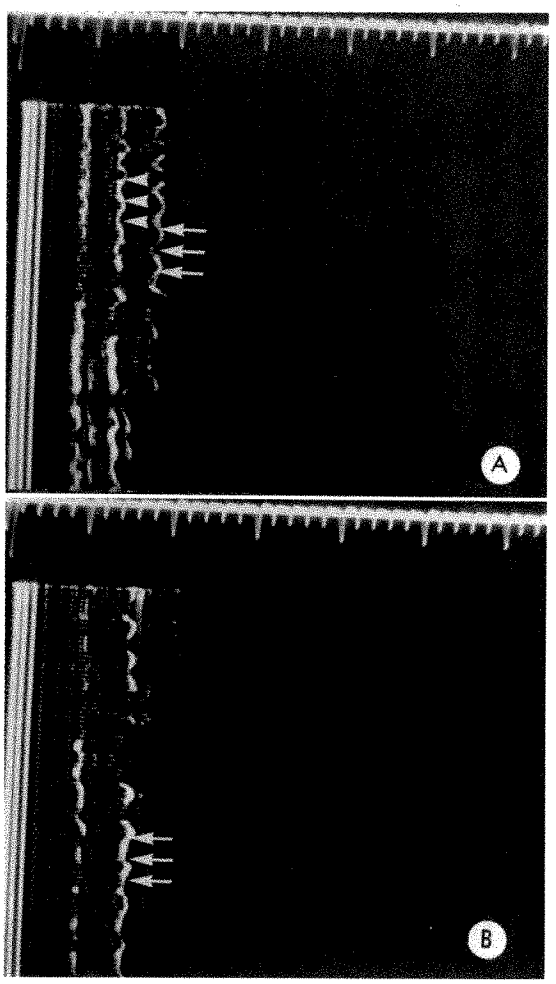


FIG. 11. (*A* and *B*) Non-subdural variant of 3:2 pattern. The patient had intracerebral bleeding. The outer echo (arrows) asymmetry is less than 3 mm. Arrowheads indicate the gray-white matter interface.

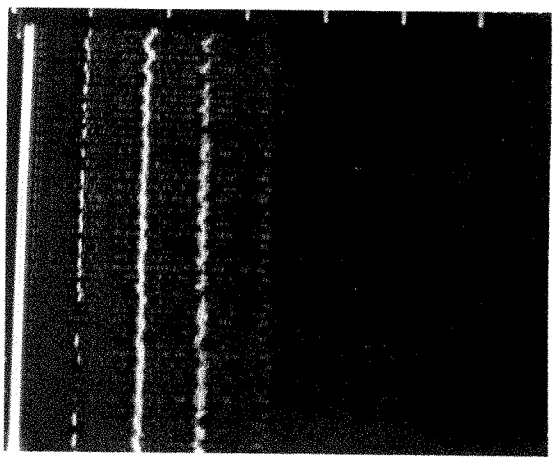


FIG. 12. This is an artifactual reverberation pattern. Note the characteristic equidistant spacing of the lines with intensity diminished in the deepest echoes.

used as controls. Three had intracranial mass lesions. Forty-two patients showed the normal 2:2 pattern. Two patients (B_2) showed a normal variant 2:1 pattern. This pattern cannot be explained. The exceptions were 2 patients with bilateral dilated ventricles (a B_1 a. trauma patient suspected of having a subdural hematoma and a C a. normal control) who showed 3 echoes on both sides, a pattern indistinguishable from subdural Pattern 1, indicating the presence of a bilateral subdural hematoma. Ten of 11 unilateral subdural hematomas (A) were diagnosed correctly by their 3:2 pattern or its variations and an asymmetry between the final echoes greater than 3 mm. In the 1 case (out of 10) in which bilateral dilated ventricles coexisted with a unilateral subdural hematoma, the ventricles did not obscure the basic 3:2 pattern which made the diagnosis; however, an atypical pattern was produced in which the second echo was

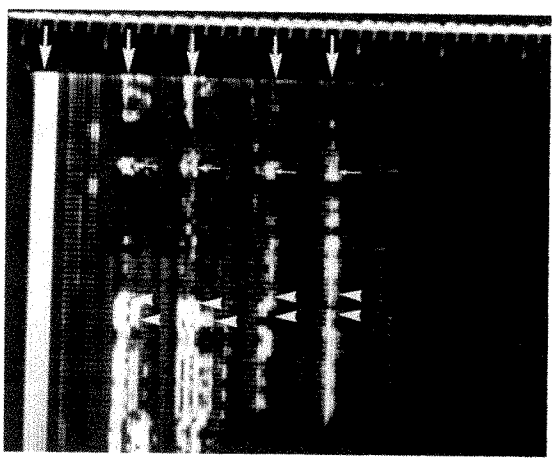


FIG. 13. Artifactual Pattern, 4 dense interrupted or solid lines appearing and disappearing simultaneously (small arrows and arrowheads). The spacings between the "main bang" and Line 1 and between Lines 2 and 3 are identical, as are the distances between Lines 1 and 2, and Lines 3 and 4.

TABLE III

COMPARISON OF ANGIOGRAPHIC AND ECHOENCEPHALOGRAPHIC FINDINGS

Type by Angiographic Criteria	Side	Maximum Angiographic Size and Location (mm.)	Echo Pattern Asymmetry (mm.)	Pattern 2 Width of "Fill-in" (mm.)	Pattern 1 and 1′ Line 2 minus 1 (mm.)
Acute to chronic	L	10, frontal	10		7
Acute	L	10	12	11	
Chronic	L	15, mostly frontal	6	10	
Acute	L	12, infratemporal	7	10	
Acute	L	38 cc. 12 cc. taps	15	10	
Chronic	L	estimated at greater than 20, very large at operation	5	17	
Chronic*	L	25, parietal	12		
Acute to Subacute	R	5, parietal	7		7
Subacute	L	15	6		6
Chronic	R	1.4 cm. shift of the anterior cerebral artery, temporo-parietal	10		6
Subacute	R	7, parieto-temporal	9		8
Bilateral	R & L	10 and 5	4		11

* 1 misdiagnosed as to side, with an atypical pattern.

split into 2 echo paths and weaker echoes were found surrounding the third echo. One unilateral subdural hematoma had an abnormal pattern which suggested a lesion contralateral to the subdural hematoma as shown in Figure 14, *A* and *B*. The one bilateral subdural hematoma was diagnosed by asymmetry alone which established a baseline allowing us to diagnose a bilateral reaccumulation of fluid (hygroma) 3 weeks later. The subdural hematomas studied included all stages of development from the acute to the chronic by angiographic criteria (Table III); our pictures could not definitely distinguish the age of the lesion. The importance of using 5 probe positions to avoid missing loculated collections cannot be overemphasized.

SUMMARY

Subdural hematomas can be diagnosed by ultrasonic space-averaging B mode scanning using a focused transducer. There are 3 criteria for diagnosis of subdural hematomas of the Type I Pattern:

1. The appearance of the "subdural pressure line" (3:2 pattern) between the normal brain-cerebrospinal fluid and the gray-white matter line.
2. An asymmetry of greater than 3 mm. between the gray-white matter line on either side.
3. Absence of "midline echoes" at 7–8 cm. on the subdural hematoma side.

In Type II there is a mass of vertical echoes or pressure lines in the general area

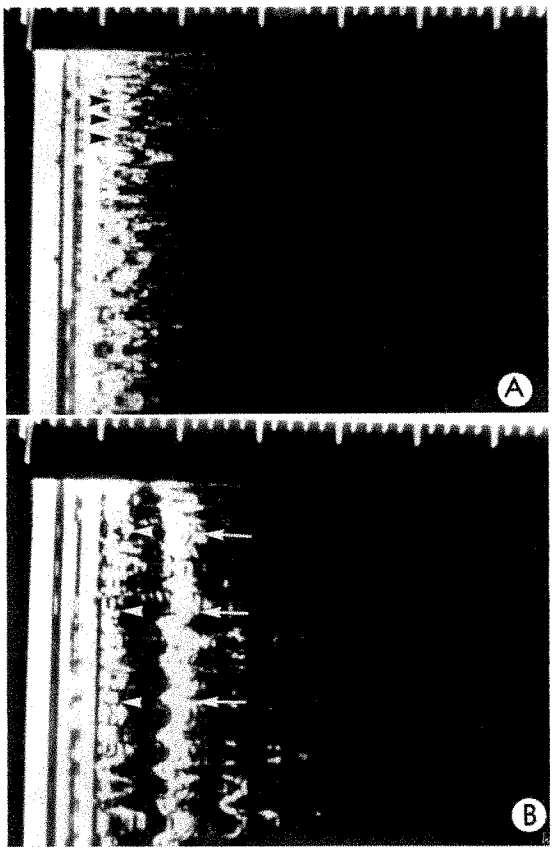


FIG. 14. (*A*) The patient had a 25 mm. subdural hematoma on the side shown in this picture. No 2 clear interfaces are visible and a horizontal "fill-in" pattern (arrowheads) extends beyond the inner table-brain cerebrospinal fluid complex. (*B*) Normal side of same patient. Arrowheads show a diffuse solid irregular line deep to the inner table-brain cerebrospinal fluid complex. Arrows show an intense interface, the origin of which is unknown.

of Lines 2 and 3. The 2nd and 3rd criteria for Type I are also satisfied.

The size of the subdural hematomas correlated well with the asymmetry up to a subdural hematoma of 1 cm. by angiography. The sensitivity of the method, *i.e.*, its ability to diagnose small subdural hematomas, seems to be greater than any method that evaluated midline shift. Large subdural hematomas above 1 cm. were indicated by a filling in of various areas. Among these the area of vertical echoes in the Type II pattern correlated best with size. The size of the remaining subdural hematomas still correlated best with the asymmetry.

Of the 60 patients examined, 12 had subdural hematomas. Eleven were diagnosed as having subdural hematomas on the correct side. One patient did not have a diagnostic picture but exhibited an abnormal pattern on the side contralateral to the subdural hematoma. Among the trauma and normal patients 1, with a 3:3 symmetric pattern, was shown by pneumoencephalography to have bilateral dilated ventricles. This shows that asymmetry is absolutely necessary for diagnosis. Those patients with intracerebral bleeding showed a normal or a 3:2 pattern distinguishable from the subdural hematoma pattern by asymmetry. The tumor also showed a 3:2 pattern different from the subdural pattern.

We feel that this technique of identification of subdural hematomas is valuable for screening purposes in the emergency room and that it may be made even more accurate with improved instrumentation.*

Jeffrey Rothman, M.D.
Columbia Presbyterian Hospital
622 West 168th Street
Box 33
New York, New York 10032

REFERENCES

1. ADAPON, B. D., CHASE, N. E., KRICHEFF, I., and BATTISTA, A. Cerebral ultrasonic tomography. *Radiology*, 1965, *84*, 115–121.
2. AMBROSE, J. Pulsed ultrasound; illustrations of clinical applications. *Brit. J. Radiol.*, 1964, *37*, 165–178.
3. DREESE, M. J., and NETSKY, M. G. Studies of lateral reflections in echo-encephalogram. *Neurology*, 1964, *14*, 521–528.
4. ELIZONDO-MARTEL, G., and GERSHON-COHEN, J. Medical ultrasonics; essentials of echoencephalography. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1965, *95*, 791–802.
5. FORD, R., and AMBROSE, J. Echoencephalography; measurement of position of mid-line structures in skull with high frequency pulsed ultrasound. *Brain*, 1963, *86*, 189–196.
6. GALICICH, J. H., LOMBROSO, C. T., and MATSON,

* This study was done with one machine which has been carefully calibrated by Hoffrel, Inc. for reproducibility of results.

D. D. Ultrasonic B-scanning of brain. *J. Neurosurg.*, 1965, *22*, 499–510.

7. GORDON, D. Echoencephalographie. *Rev. neurol.*, 1958, *99*, 652–653.
8. JEPPSON, S. Echoencephalography. *Acta chir. scandinav.*, 1961, Suppl. 272, pp. 1–151.
9. LEKSELL, L. Echo-encephalography: detection of intracranial complications following head injury. *Acta chir. scandinav.*, 1955, *110*, 301–309.
10. LITHANDER, B. Clinical use of echo-encephalography. *Acta psychiat. et neurol. scandinav.*, 1960, *35*, 241–244.
11. LITHANDER, B. Clinical and experimental studies in echo-encephalography. *Acta psychiat. et neurol.*, 1961, Suppl. 159, 1–53.
12. LITHANDER, B. Origin of echoes in echoencephalogram. *J. Neurol., Neurosurg. & Psychiat.*, 1961, *24*, 22–31.
13. SCHIEFER, W., KAZNER, E., and BRÜCKNER, H. Die Echoenzephalographie, ihre Anwendungsweise und klinischen Ergebnisse. *Fortschr. Neurol. & Psychiat.*, 1963, *31*, 457–491.
14. TANAKA, K., and WAGAI, T. Ultrasonic diagnosis of brain disease in Japan. Chapter 16. In: Ultrasound as a Diagnostic and Surgical Tool. Editor, D. Gordon. Williams & Wilkins Company, Baltimore, 1964, p. 161.
15. TER BRAAK, J., GRANDIA, W., and DE VLIEGER, M. Echoencephalography as aid in diagnosis of subdural and extradural hematomas. In: Recent Neurological Res. Elsevier Press, Inc., Amsterdam, 1959, 37–45.
16. DE VLIEGER, M. Echoencephalography and extracerebral hematomas. Chapter 15. In: Ultrasound, as a Diagnostic and Surgical Tool. Editor, D. Gordon. Williams & Wilkins Company, Baltimore, 1964, p. 145.
17. DE VLIEGER, M. and RIDDER, H. J. Use of echoencephalography. *Neurology*, 1959, *9*, 216.
18. WAGAI, T., and TSUCHIDATE, M. Recent Advances of Medical Application of Ultrasound. Developed by the Ultrasonic Research Group, Juntendo University, Tokyo, 1963.
19. WAGAI, T., MIYAZAWA, R., KAZUBUMI, I., and KIKUCHI, Y. Ultrasonic diagnosis of intracranial disease, breast tumors and abdominal diseases. Chapter 23. In: Ultrasonic Energy; Biological Investigations and Medical Applications. Editor, E. Kelly. University of Illinois Press, Urbana, 1965, p. 346.

B-SCAN ULTRASOUND EXPLORATION OF NEOPLASTIC DISEASE*

By BRUNO DAMASCELLI, M.D., FRANCA FOSSATI, M.D., TITO LIVRAGHI, M.D., *and* ALDO SEVERINI, M.D.
MILAN, ITALY

IT IS established that high frequency ultrasound waves emitted by special crystals in the form of ultrashort pulses can be used for obtaining physical and morphologic information on the intrinsic structures of some internal organs or body regions. [1,7–13,15]

The echoes reflected by the tissues are recorded either one- or two-dimensionally. One-dimensional representation (A mode display) is routinely used in echoencephalography and for fetal biparietal measurements and can be of help in the search for calculi in the bile ducts and ureters.[17] This method can be applied only when the position of the interfaces is known or can be reasonably assumed.[4,16,19] Two-dimensional representation (B mode display) now has a wide range of clinical applications and its message is more immediate, since the anatomy of the section of the body being scanned can be recognized at once. But the technique is more complex, the equipment more costly and the interpretation of the images a matter of considerable skill.[2,6,7]

This paper is concerned with a preliminary experiment with two-dimensional echography in the study of neoplastic diseases of various sites and some examples are quoted by way of illustration (Fig. 1–18).

EQUIPMENT AND METHODS

The sonar we use is the Diasonograph supplied by Smith Industries, Ltd. We have modified some minor points in the recommendations of Donald and Brown[5] regarding the use of the equipment: the coupling medium flows continuously between crystal and skin; the pulse repetition frequency is kept as high as possible, *i.e.*, 750 pulses/sec.; the organs in the hypochondriac region are examined in apnea; and the brilliance of the cathode screen is kept as low as possible. We have found that

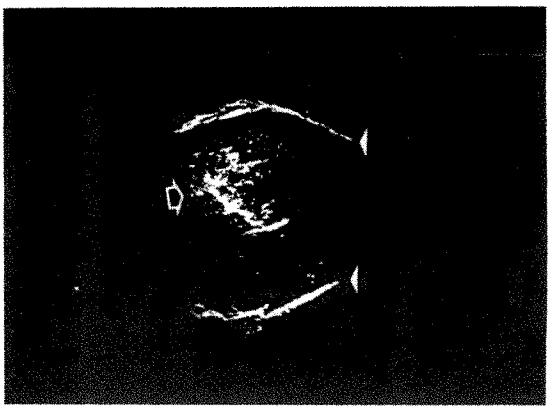


FIG. 1. Horizontal section of the skull taken 1.5 cm. above the external auditory meatus. A cerebral astrocytoma arising from the right temporal lobe produces pathologic echoes marked by the arrow to the left of the observer. The 2 marks on the right of the Figure correspond to the position of the theca, proximal to the transducer above and distal below (1.5 MHz).



FIG. 2. A partly cystic macrofollicular adenoma of the thyroid gland appears as a circular image immediately under the echo of the skin and above the anterior wall of the trachea, which is marked by an arrow. Transverse section of the neck (5 MHz).

* From the Institute of Radiology, University of Milan, and the National Cancer Institute of Milan, Italy.

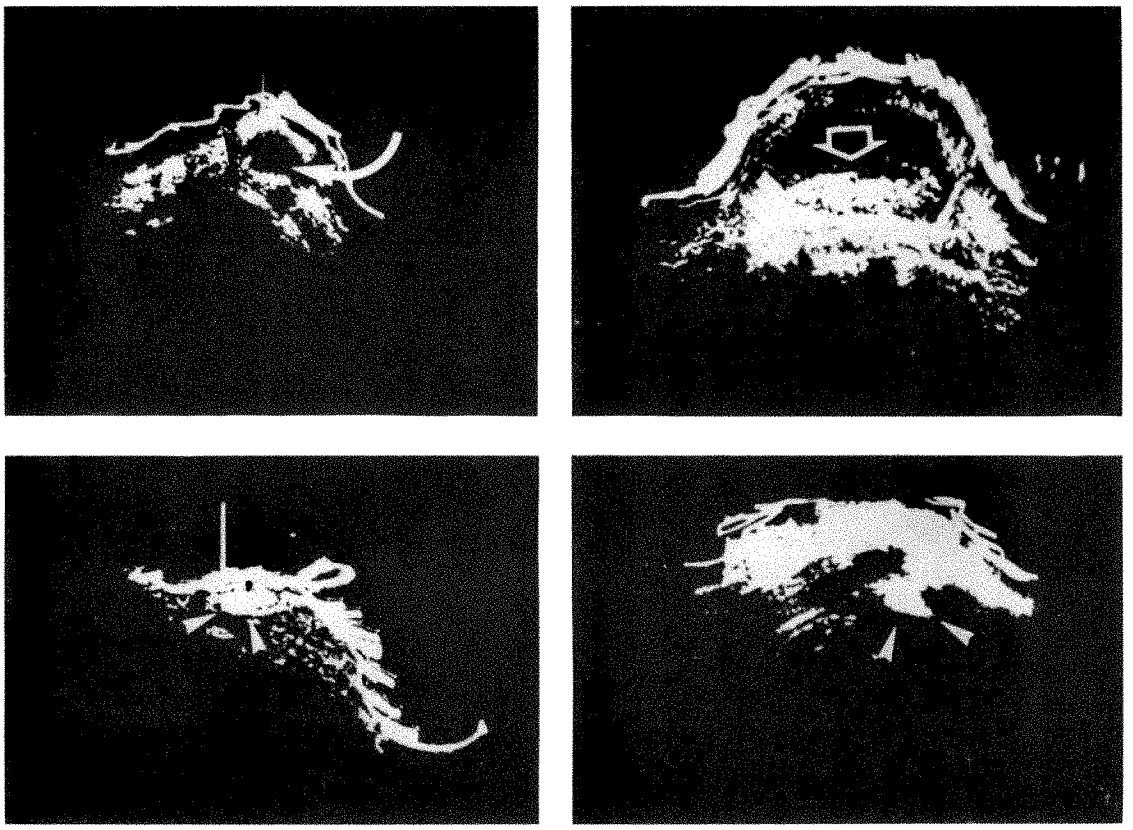


Fig. 3. Four different cases of breast tumors: from top left to bottom right: a cyst, a cystosarcoma phylloides, a fibroadenoma, and a carcinoma. All the sections are longitudinal. The homogeneous contents of the cyst are marked by the arrow; the arrow inside the phylloid tumor marks the solid part of the tumor overlying the fluid part (transonic). The 2 small marks inside the fibroadenoma and carcinoma indicate the inward-facing part of the tumors. The carcinoma, which was at an advanced stage, was adherent to the skin (5 MHz)



Fig. 4. Transverse section of the chest (supine position) at the level of the 4th intercostal space in a patient suffering from a reticulosarcoma of the left lung with profuse pleural effusion. The arrows on the observer's right mark the pathologic echoes due to the disease (top) and a reflection of the posterior wall of the chest (bottom). The arrow on the observer's left indicates the inside of the heart (1.5 MHz).

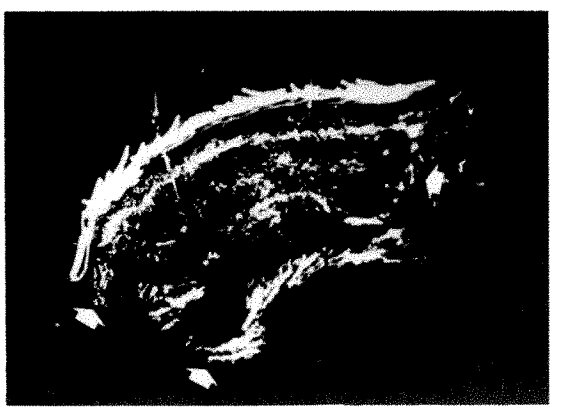


Fig. 5. Transverse section of the liver in a case of metastasis from breast cancer. The arrows to the left of the observer mark the 2 opposite surfaces of the liver at the level of the right lobe. Between them lie numerous echoes that are not normally visible; they are due to the neoplastic tissue, which interferes with the normal acoustic properties of the liver. The arrow on the observer's right indicates the margin of the left lobe (2.5 MHz).

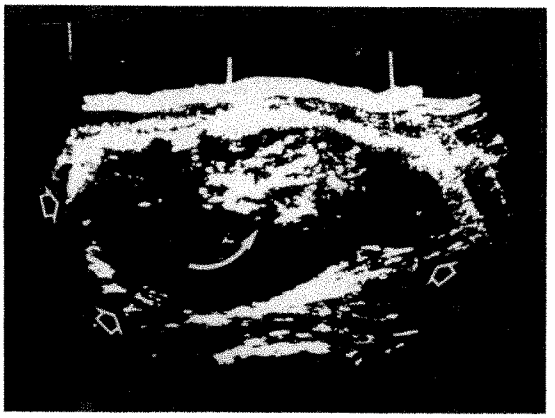


FIG. 6. Primary carcinoma of the liver; longitudinal section in the midclavicular line. The liver is enormously enlarged; the vertical traces at the top, left to right, represent the positions of the costal arch, the umbilical line and the cutaneous projection of the anterior margin of the liver, which is marked by the arrow on the observer's right; the arrows on the observer's left are located around the cranial side of the organ. The arrow inside indicates pathologic echoes due to the tumor (1.5 MHz).

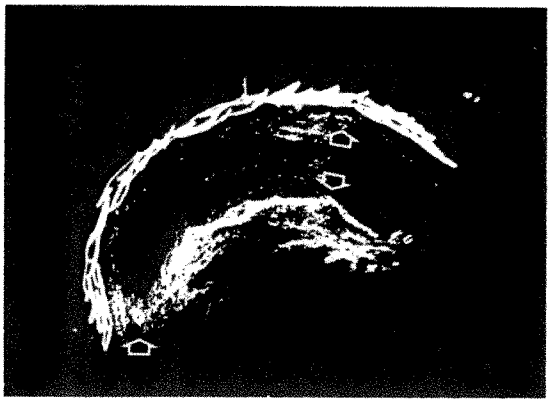


FIG. 7. Enormous splenomegaly due to lymphosarcoma. Transverse section of the abdomen with the patient in the left anterior oblique position. The organ virtually crosses the whole abdominal cavity; the arrow on the observer's left indicates the medial margin of the spleen and the 2 arrows on the right (inside) the 2 opposite surfaces (2.5 MHz).

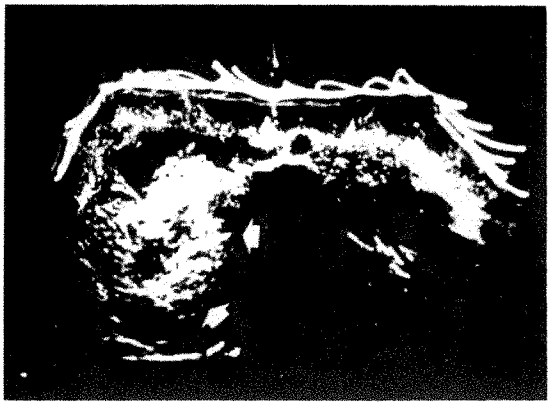


FIG. 8. Transverse section of the abdomen slightly below the epigastrium; the arrows mark the echoes due to a large hypernephroma starting from the right kidney; the tumor coexisted with hydronephrosis; it appears under a transonic space due to part of the right lobe of the liver (2.5 MHz).

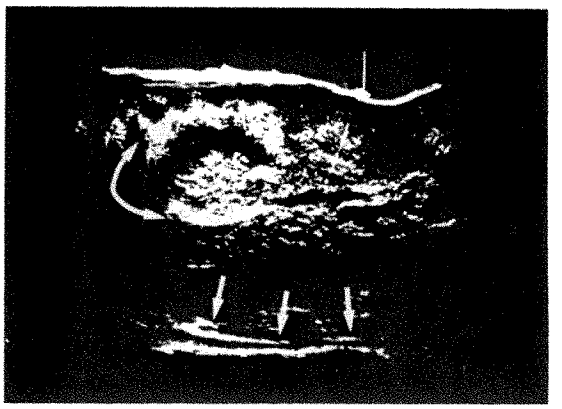


FIG. 9. Longitudinal section of the abdomen to the right of the midline (prone position) in a case of right adrenal neuroblastoma. The large tumor is marked by the arrow on the observer's left; the 3 arrows at the bottom mark the anterior aspect of the liver (2.5 MHz).

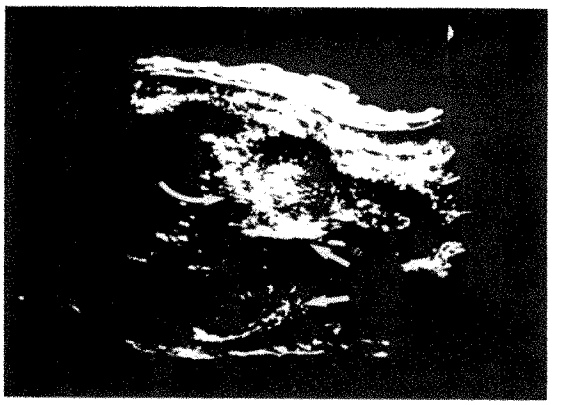


FIG. 10. Longitudinal section of the abdomen of the same case as in Figure 9, taken 1 month after treatment with cyclophosphamide. The decrease in the size of both tumor and liver is already evident (2.5 MHz).

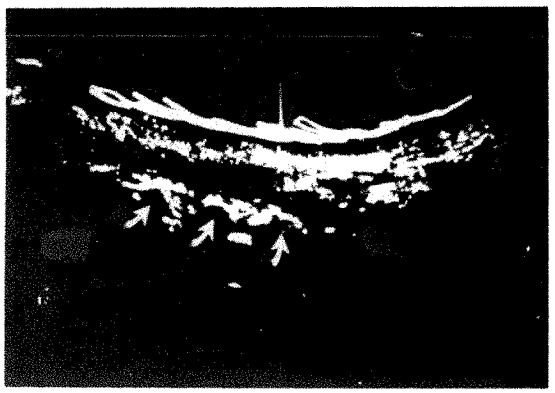


FIG. 11. Longitudinal section of the abdomen immediately to the right of the midline. Numerous polycyclic echoes are present near the posterior wall (arrows); this patient had large lumbo-aortic lymph nodes due to chronic lymphatic leukemia. The vertical reference at the top marks the position of the umbilical line (2.5 MHz).

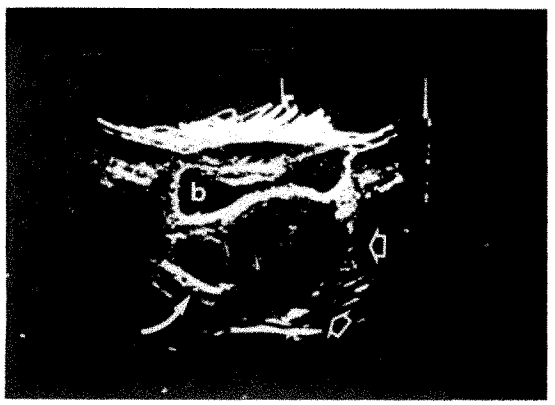


FIG. 12. Transverse section of the abdomen slightly above the symphysis pubis. A uterine fibroid consisting of 2 nodules, the larger on the observer's right (arrows), raises the fundus of the bladder (b), which is distended with urine; the bladder appears to be compressed and deformed (1.5 MHz).

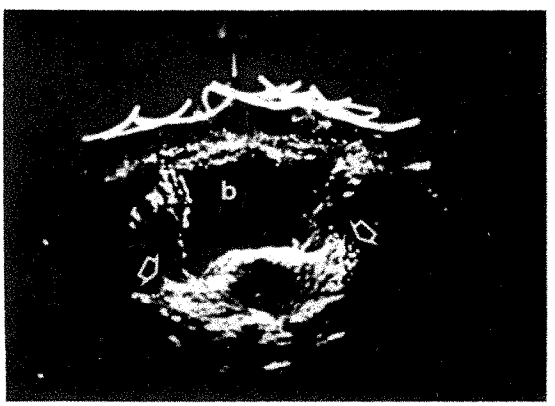


FIG. 13. Stage IV uterine carcinoma. Transverse section of the abdomen just above the symphysis pubis. Below the bladder the uterus appears as a transonic circular image of greater than normal size. On both sides are numerous echoes not usually observed (arrows). Note the very low gain-setting. Both parametrial ligaments are in fact infiltrated. b = distended bladder (2.5 MHz).



FIG. 14. Hydatidiform mole that had developed at the 10th–11th week of pregnancy. Longitudinal section of the abdomen. Numerous echoes are observed (arrow) in the uterine cavity; the embryo is unrecognizable (compare with the next figure). The echographic findings are typical (2.5 MHz).

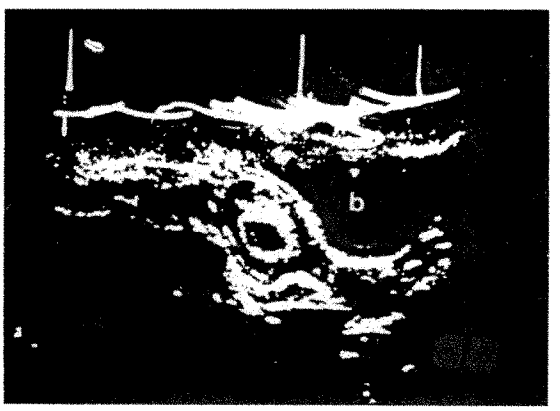


FIG. 15. Longitudinal section of the abdomen in the midline. A normal pregnancy at the 7th–8th week of amenorrhea appears as a circular image inside the uterus (embryonal sac) on the anterior side close to the fundus. b = bladder fully distended by urine (2.5 MHz).

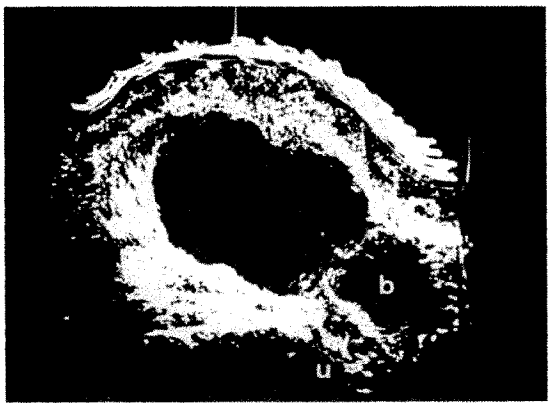


FIG. 16. Longitudinal section of the abdomen immediately to the left of the midline. A large unilocular serous cystoma of the left ovary occupies a large part of the lower abdomen. b = distended bladder; u = position of the uterus (2.5 MHz).

these factors are very important for good detail on Polaroid film. For examining the abdomen, 2.5 MHz is normally used, 1.5 MHz is more suitable for the skull and chest, and 5 MHz is nearly always necessary for the thyroid and breast. Sensitivity control is always tricky and the right value has to be found by trial and error in the course of the investigation. The electric energy applied to the probe at the maximum gain-setting value is 2.7 millijoules per impulse and at the minimum value is 0.37 millijoules per impulse. As there is always incomplete contact between probe and patient, the sonic energy actually transmitted is bound to be considerably below these values.

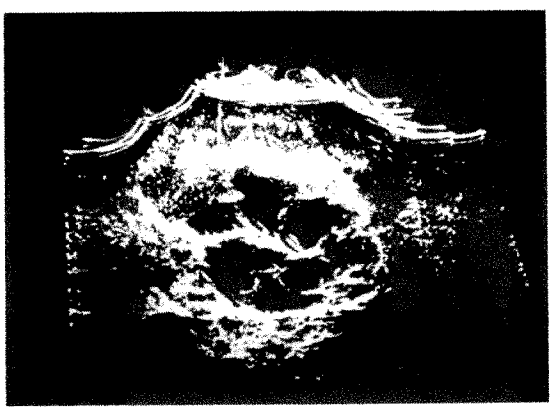


FIG. 17. Multilocular Brenner tumor arising from the right ovary. Transverse section of the abdomen halfway between the bi-iliac line and the symphysis pubis with the transducer at an angle of 30° to the caudocranial axis. The intrinsic structure of the tumor is clearly evidenced (2.5 MHz).

CASE MATERIAL

A total of 197 patients was selected from our case material; nearly all had tumoral lesions of various sites and the diagnosis at the time of ultrasound scanning was in many cases known or there was presumptive clinical evidence. The investigation was done blind in only 22 cases: in 2 cases of reticulosarcoma of the lungs, where pleural effusions obstructed roentgen visualization of the parenchymal alterations, and in 20 cases of lumbo-aortic lymphadenopathy in which lymphography had not been carried out.

In all the cases summarized in Table 1 the diagnosis was based on clinical, radiologic (including angiography and radioactive isotope scanning) and laboratory findings. Of the 197 cases in this Table the following were verified at operation: the cerebral astrocytoma; all the thyroid (11 adenomas, 2 carcinomas), breast (6 benign, 7 malignant) and ovarian tumors (13 benign, 7 malignant); 15 fibromyomas of the uterus (of the 30 uterine tumors, including 15 Stage III and IV cancers); 2 of the 8 cases of splenomegaly (all secondary to systemic blood and lymph diseases); both

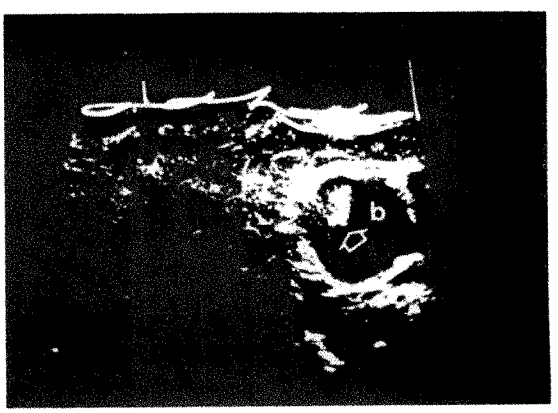


FIG. 18. Vegetating carcinoma of the bladder (arrow inside b = bladder distended by urine). Longitudinal section of the abdomen in the midline (2.5 MHz).

TABLE I

CASE MATERIAL

Type of Disease	No. of Cases	Status of Two-dimensional Ultrasound Patterns			
		Contributory	Non-contributory	Inconclusive	Error Per Cent
Cerebral astrocytoma	1	1			
Reticulosarcoma of the lung	2	2			
Bronchogenic carcinoma	1		1		
Thyroid tumors	13	5	4	4	
Breast tumors	13	6	5	2	
Fibromyxosarcoma of the thigh	1	1			
Synovial sarcoma of the leg	1	1			
Abdominal masses					
liver	53	32	9	12	
spleen	8	8			
kidney	7	6	1		
adrenal neuroblastoma	1	1			
retroperitoneal lymph-adenopathy	44	27	6	11	
uterine tumors	30	21			
ovarian tumors	20	20			
bladder tumors	2	2			
Total	197	133	30	34	32

cases of sarcoma of the soft tissues of the limbs; 3 of the cases of renal masses (1 cyst, 1 hypernephroma, 1 hydronephrosis secondary to calculosis), whereas of the 4 remaining cases, 3 were due to hydronephrosis secondary to parametrial infiltrations of a cervical carcinoma and 1 to multiple cysts of both kidneys. Of the 53 cases of hepatomegaly, 9 were simple, 25 were due to secondaries of tumors of variable origin, 18 exhibited liver damage from systemic blood and lymph diseases and 1 case had a primary cancer of the liver. Ten of the 44 cases of retroperitoneal lymph-adenopathy were metastatic and 34 were due to systemic blood and lymph diseases. Direct lymphography was done in all these cases.

RESULTS

As mentioned earlier, in nearly all our patients the disease had been diagnosed on the basis of instrumental and laboratory evidence, or at least a general diagnosis was obvious on clinical grounds. Therefore, in Table 1 we have not used the word "diagnosis," but have classified the information supplied by two-dimensional echography simply as "contributory," "noncontributory," or "inconclusive" in relation to the solution of the clinical problem.

The sonar images were rated contributory in the following circumstances:

(1) when the disease was evidenced in general both by the reflected ultrasounds and by all the other investigations taken together, the latter not having led to an absolutely precise diagnosis;
(2) when the results of two-dimensional echo sounding were complementary to those of other diagnostic procedures; and
(3) when the method proved to be actually more helpful in elucidating the clinical problem.

In evaluating Points 2 and 3 we considered the relative complexity of other instrumental investigations compared to the

TABLE II

TYPE OF INFORMATION SUPPLIED BY TWO-DIMENSIONAL ULTRASOUND EXPLORATION IN THE CASES IN WHICH THE INVESTIGATION WAS CONTRIBUTORY

Disease	No. of Cases	General	Complementary	More Precise
Lower limb sarcomas (2) Cerebral astrocytoma (1) Lung reticulosarcomas (2)	5	5 abnormal echo patterns		
Thyroid tumors	5	5 presence of tumor		
Breast tumors	6	3 presence of tumor	2 evidence of cyst	1 good correlation with gross pathology (cystosarcoma phylloides)
Abdominal masses				
liver	32		32 liver enlargement with abnormal echo patterns	
spleen	8	8 enlargement of spleen		
kidney	6		3 hydronephrosis 1 bilateral polycystic disease 1 cyst	1 hydronephrosis with non-functioning kidney on excretory urogram
right adrenal neuroblastoma	1			1 presence of tumor, probably retroperitoneal
para-aortic lymphadenopathy	27		27 abnormal echo patterns near posterior wall of abdomen	
uterine tumors	21	8 parametrial infiltrations	12 fibroids	1 hydatidiform mole with typical finding
ovarian tumors	20		16 presence of uni- or multiloculated tumor	4 multiloculated cystic tumor in clinically suspected fibroid
bladder tumors	2	2 presence of tumor		
Total	133	31	94	8

simplicity of ultrasonic echo sounding. To give an example, the patient suffering from neuroblastoma arising in the right adrenal gland was studied by urography, retroperitoneal pneumography and abdominal aortography, but the echography, done before the last named investigation, had already identified the site and size of the tumor and had guided the transcutaneous needle biopsy.

Ultrasound echography is also an easy procedure for long-term follow-up after chemotherapy.

Table II shows the three grades of "contributions" of the positive results.

The diseases that yielded silent sonograms, false positives or false negatives, or were in any way misleading, are classified as such in Table III.

The findings classified as inconclusive (Table I) were all the outcome of poor quality recordings, and in a few cases the human element came into play too: the operator was not "in form," took too few sections, or failed to find the optimum sensitivity control value.

CONCLUSIONS

Ultrasound exploration is now being used widely in the clinical field because it is a safe diagnostic procedure, and there are many examples in the literature of the kind of morphologic information that can be supplied by this method.

TABLE III

STATUS OF NONCONTRIBUTORY RESULTS OF B-SCAN ULTRASOUND DISPLAY

Disease	No. of Cases	False Positives	False Negatives	Useless
Bronchogenic carcinoma	1		1 no evidence of disease	
Thyroid tumors	4		1 no evidence of disease	3 incorrect conclusions
Breast tumors	5		3 no evidence of disease	2 incorrect conclusions
Abdominal masses				
liver	9	9 echo patterns in liver with negative needle biopsy and laboratory findings		
kidney	1			1 incorrect conclusion
uterine tumors	4		2 no evidence of parametrial infiltration	2 incorrect conclusions
para-aortic lymphadenopathy	6	6 para-aortic echoes with normal lymphangiography (artifacts)		
Total	30	15	7	8

The results that we have obtained with two-dimensional echography have, in the main, been confirmatory, except for the demonstration of retroperitoneal lymph node disease and of parametrial infiltrations by cervical cancer, of which we had no prior information. We must, however, admit that in nearly all the cases in which two-dimensional echo sounding was done, the disease was known or could be appreciated clinically. If we take the noncontributory and inconclusive results together, there is no escaping the fact that no conclusion of practical value was reached in over a quarter of our cases (error rate = 32 per cent). In only 8 cases did ultrasound exploration yield better diagnostic information than the clinical examination and instrumental investigations taken together. Against this must be considered the simplicity, safety and repeatability of the examination. The highest error rate was in small lesions, such as tumors of the thyroid or breast, and in certain body regions, such as the central quadrants of the abdomen, where artifacts are likely because of intestinal loops and the presence of gas. Air, of course, tends to reflect all sound and so it is necessary to use very high gain-setting on the energy beam.

When the hypochondriac organs are enlarged they yield very picturesque ultrasonograms, but differential diagnosis is an arduous task when intrinsic lesions are present. In a previous paper we pointed out that it is hardly ever possible to state whether abnormal echoes in the liver are typical for a given disease; the most that can be said is whether a space-occupying lesion is cystic or solid.[3] In the case of clinically suspected liver metastases, two-dimensional echo sounding seems to support liver scintiscanning, but here again greater experience is needed. The inconclusive rate is high and in 9 cases in which exploration yielded a misleading result all were false positives.

Taking the indications considered as a whole, we are inclined to think, although not all workers would agree,[18] that the type of information supplied by ultrasounds is general, except in tumors of the uterus, such as fibromas, or of the ovaries, in the majority of which the technique has genuine diagnostic possibilities. It is widely held that ultrasounds are particularly useful in examination of the female pelvis, but we feel that the sonar operator's judgment is all too often influenced by the clinical findings.

So far two-dimensional echography seems to have yielded definitive, competitive results only in the study of the early stages of pregnancy and in complications of pregnancy, for which no other indirect method of equal safety has yet been found.[14]

To sum up, it is our personal conviction that this mode of representation of the echoes reflected by the soft tissues, which is ideally suited to preliminary diagnostic investigation, is still in its infancy and that better instruments and more experience are needed before the structures of the intact human body can be analyzed accurately.

SUMMARY

The two-dimensional ultrasound technique of Donald and Brown was used for examination of 197 patients, nearly all suffering from neoplastic lesions at various sites.

The method proved to be contributory in 133 cases, but it is stressed that the disease was nearly always known or the clinical evidence was clear before ultrasound exploration.

If the misleading and inconclusive results are taken together, this investigation was of no advantage to diagnosis in 32 per cent of the cases.

The current limitations of the method are: the small scope for differential diagnosis and the low resolving power; small lesions are missed or are obscured by artifacts. Hence, the need for better instruments and more experience.

In view of the safety, simplicity and repeatability of the investigation it is thought that the necessary technologic improvements will soon be forthcoming, and that this method will prove to be an ideal preliminary diagnostic procedure.

Bruno Damascelli, M.D.
Institute of Radiology
University of Milan
Piazzale Gorini 22
20133 Milan, Italy

The authors wish to thank Professor A. Ratti, Head of the Institute of Radiology, University of Milan, and Professor Ian Donald of Glasgow University for continuous help and encouragement, and Dr. Nella Guidi, Miss P. Hyde, Mr. M. Damascelli, and Mr. G. Damascelli for their tireless cooperation.

REFERENCES

1. BRINKER, R. A., KING, D. L., and TAVERAS, J. M. Echoencephalography. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1965, *93*, 781–790.
2. BROWN, T. G. Direct contact ultrasonic scanning techniques for visualization of abdominal masses. Proceedings of the Second International Conference on Medical Electronics, Paris, June, 1959. Medical Electronics. Iliffe & Sons, London, pp. 358–366.
3. DAMASCELLI, B., BONADONNA, G., USLENGHI, C., RONCORONI, L., and VERONESI, U. Two-dimensional ultrasounds in diagnosis of liver diseases. *J.A.M.A.*, 1968, *204*, 963–968.
4. DONALD, I. Presentation of methods of ultrasonic echo sounding information from tissue interfaces. Proceedings of the Symposium held in Glasgow, September, 1964. Biomechanics and Related Bioengineering Topics. Pergamon Press, 1965, pp. 47–61.
5. DONALD, I., and BROWN, T. G. Demonstration of tissue interfaces within body by ultrasonic echo sounding. *Brit. J. Radiol.*, 1961, *34*, 539–546.
6. DONALD, I. Ultrasonography in two dimensions. *Med. Biol. Illinois*, 1964, *14*, 216–224.
7. DONALD, I. Diagnostic uses of sonar in obstetrics and gynaecology. *J. Obst. & Gynaec. Brit. Emp.*, 1965, *72*, 907–919.
8. DONALD, I., and ABDULLA, U. Further advances in ultrasonic diagnosis. *Ultrasonics*, 1967, *5*, 8–11.
9. FEIGENBAUM, H., WALDHAUSEN, J. A., and HYDE, L. P. Ultrasound diagnosis of pericardial effusion. *J.A.M.A.*, 1965, *191*, 711–714.
10. GOLDBERG, B. B., OSTRUM, B. J., and ISARD, M. Ultrasonic aortography. *J.A.M.A.*, 1966, *198*, 119–124.
11. HOLMES, J. H., and HOWRY, D. H. Ultrasonic diagnosis of abdominal disease. *Am. J. Digest. Dis.*, 1963, *8*, 12–32.
12. HOLMES, J. H. Ultrasonic diagnosis of lesions of liver. In: Diagnostic Ultrasound. Proceedings of the First International Conference. Plenum Press, New York, 1966, pp. 249–263.
13. HOLMES, J. H. Ultrasonic studies of bladder. *J. Urol.*, 1967, *97*, 654–663.
14. VON MICSKY, L. I. Ultrasonic tomography in obstetrics and gynecology. In: Diagnostic

Ultrasound. Plenum Press, New York, 1966, pp. 348–368.
15. Moss, A. J., and Bruhn, F. Echocardiogram: an ultrasound technic for detection of pericardial effusion. *New England J. Med.*, 1966, *274*, 380–384.
16. Ostrum, B. J., Goldberg, B. B., and Isard, H. J. Mode ultrasound differentiation of soft-tissue masses. *Radiology*, 1967, *88*, 745–749.
17. Report of the Medical Ultrasound Research Center, Juntendo University, Ongo, Tokyo, 1965.
18. Shigemitsu, M., Takenchi, H., and Nakano, K. Diagnostic application of ultrasound in obstetrics and gynecology. In: Diagnostic Ultrasound. Plenum Press, New York, 1966, pp. 452–464.
19. Sugar, O., and Vematsu, S. Use of ultrasound in diagnosis of intracranial lesions. *S. Clin. North America*, 1964, *44*, 55–64.



ECHOGRAPHIC DIAGNOSIS OF RETROPERITONEAL LYMPH NODE ENLARGEMENT*

ULTRASOUND SCANNING TECHNIQUE AND DIAGNOSTIC FINDINGS

By W. MICHAEL ASHER, M.D.,† *and* ATIS K. FREIMANIS, M.D.‡
COLUMBUS, OHIO

THE purpose of this study was to investigate whether echo scanning can provide useful information about retroperitoneal lymph node enlargements and other retroperitoneal masses, particularly in the diagnosis of lymphoma. Our results show that such diagnostic information can indeed be obtained. This report will describe the method, possibilities and limitations of echography of the abdomen in patients with lymphomatous diseases.

Diagnostic ultrasound (echography) is a proven valuable adjunct to conventional techniques in many fields. The two modalities available are "A" mode, which permits measurements of distances and to some extent determination of size and distribution of echoes along a linear path, and "B" mode, which gives a two dimensional presentation useful in outlining anatomic relationships.[1,3,4] It is currently the only clinically feasible method for observing cross section anatomy in the abdomen.

To our knowledge, echographic diagnosis of lymphomatous masses has not been described previously in the literature.

MATERIAL AND METHOD

To investigate lymph node enlargement, over 100 echographic scan series were obtained in 100 known or suspected (and eventually proven) lymphoma patients (Table 1). Several patients were scanned on more than one occasion.

The abdomen was scanned from below the bifurcation of the aorta to the level of the diaphragm in 3 cm. cross section increments (Fig. 1), as well as along three longitudinal sagittal planes. A Picker Ultrasonic Laminograph (Model #592500) with a 2.0 Mhz lead zirconate titanate crystal was employed in "B" mode using contact scanning. Polaroid photographs of the storage oscilloscope images were obtained at each of these levels. Mineral oil was used as an acoustic coupling agent. After interpretation of the scans, the echographic information was correlated with other diagnostic examinations such as barium gastrointestinal series, intravenous pyelograms and lymphangiograms. In 9 cases postmortem or surgical exploration was available.

The echographic representation of nor-

TABLE I

ECHOGRAM EXAMINATION

Lymphoma patients	100
Controls	230
Total	330
Echographic Findings	
Para-aortic lymph nodes enlarged	41
Para-aortic lymph nodes not enlarged	54
Inadequate examination	5
Total Lymphoma Patients	100*
Correlation	
Roentgenographic†	67
Surgery or autopsy	9
No direct confirmation	19
Inadequate examination on echogram	5
Total	100

* Twelve patients had lymphoma masses in the abdomen other than para-aortic lymph node, hepatic or splenic enlargement.
† Includes 19 lymphangiograms.

* From the Department of Radiology, Ohio State University College of Medicine, Columbus, Ohio.
Supported in full by the Public Health Service Research Grant No. 5-SO1-FR-05409-07 from the National Institutes of Health General Research Support Grant.
† Formerly: Medical Student, Ohio State University College of Medicine; now Intern, U. S. Naval Hospital, San Diego, California.
‡ Professor, Department of Radiology, Ohio State University College of Medicine, Columbus, Ohio.

mal anatomic structures was established by obtaining such scans in over 200 normal individuals or patients with nonrelated diseases (Fig. 2, *A* and *B*).

RESULTS

Enlarged para-aortic lymph nodes were diagnosed by echograms in 41 of the 100 lymphoma patients. Fifty-four were found to be free from para-aortic lymph node enlargement. Technical difficulties or physiologic problems (such as excessive intestinal gas) caused 5 echograms to be inadequate for diagnosis. Confirmation (of both positive and negative findings) was obtained by roentgen studies in 67 cases and by postmortem examination or surgery in 9 cases. In 19 cases, satisfactory roentgenologic or other confirmation of findings was not obtained at the time of the echographic examination.

In all cases, independent interpretation of the echograms and roentgenograms or clinical examination showed good agreement, with the following exceptions: Adequate roentgen examination (but without lymphangiography) failed to demonstrate a lymph node mass evident on the echogram in 3 cases. In 2 additional cases, echograms demonstrated *para-aortic* lymph node masses in areas not filled with contrast medium by conventional lower extremity lymphangiography (but proven by other roentgen examinations). In 6 cases, lymph node enlargement was not diag-

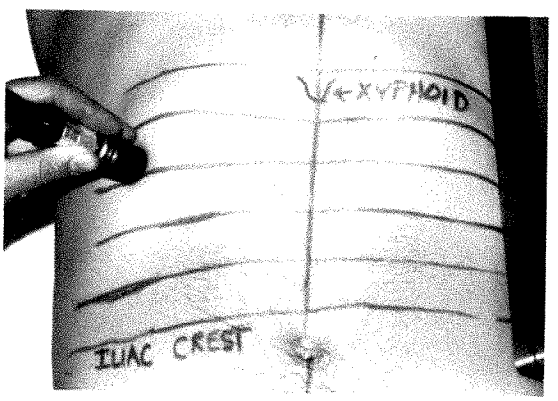


Fig. 1. Method of marking the patient prior to scanning using the iliac crest as a standard reference point. The marks, placed on the skin with water-soluble ink markers, delineate the transducer pathway for the examination. Additional marks, either up or down or to either side of the midline are used as necessary.

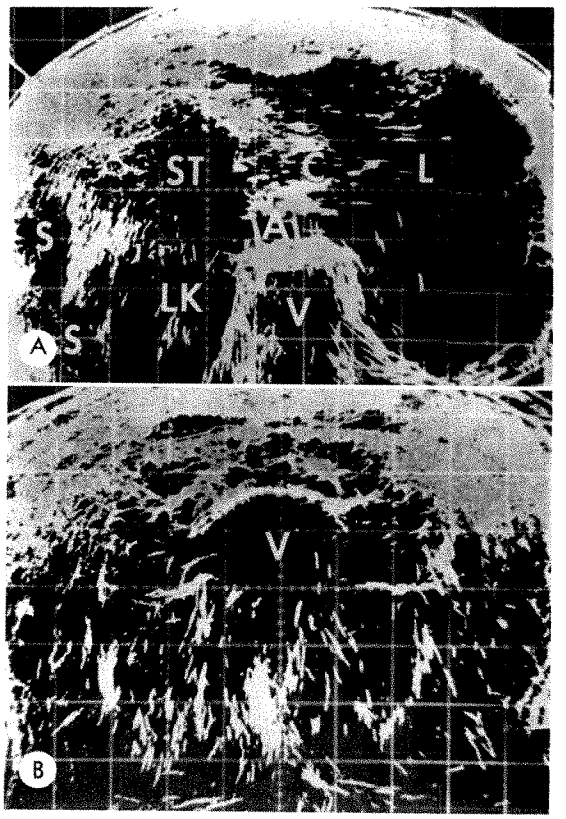


Fig. 2. Cross section echograms obtained in a normal individual. On all of the figures the transverse sections are placed so that the front of the patient is up and the right side to the reader's right. Each square on the line grid corresponds to 2 cm. in the patient. (*A*) Twelve centimeters above the iliac crest. S—spleen, LK—left kidney, ST—stomach, V—vertebral body, A—aorta, C—vena cava, L—liver. Note that the prevertebral para-aortic structures are represented by an area of echo-returning tissues in which the great vessels and the parenchymal organs appear as sonolucent structures. Lymphomatous and probably most carcinomatous lymph nodes also appear as sonolucent masses. (*B*) On a lower section of the abdomen (at the iliac crest level) the prevertebral structures are similarly demonstrated in this normal person with a grouping of scattered echoes returning from perivascular connective tissues, nerves and smaller vessels surrounding the common iliac arteries and veins just distal to the bifurcation of the aorta and vena cava (immediately anterior to the vertebra, V).

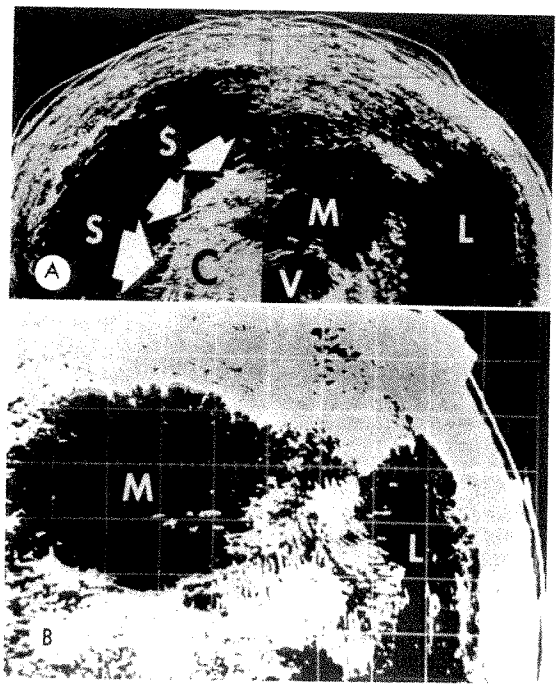


FIG. 3. (*A*) A group of markedly enlarged subhepatic lymph nodes (M) in a patient with chronic lymphocytic leukemia. The spleen (S) is characteristically enlarged. Note curved posteromedial border (white arrows). The right lobe of the liver (L) is also enlarged. Note compressed tissue effect (C) medial to spleen and the fact that the vertebral body (V) is still identified. The aortic contour merges into the lymph node mass. (*B*) Partial transverse scan at 9 cm. above iliac crest in another patient with lymphosarcoma. The large subhepatic mass (M) was shown to be within and surrounding the first and second portions of the duodenum. L—right lobe of the liver.

nosed by echogram when suspected by urographic or gastrointestinal series. However, there were no false echographic negatives in comparison to 8 positive lymphangiographic examinations. (We have encountered one such case after the conclusion of this series.) In 12 instances lymphomatous masses were noted by ultrasound in areas not normally visualized by lymphangiography. These masses were confirmed by roentgenographic studies or palpation. It is a recognized fact that lymphangiography fails to visualize lymph nodes not in the drainage path of the injected lymphatics (Fig. 3, *A* and *B*).

In the control group, lymph node enlargement (2–3 cm. in diameter) was diagnosed echographically once. At surgery, 1–2 cm. diameter lymph nodes were found in the area predicted (near the head of the pancreas), but histologic study failed to yield a diagnosis other than nonspecific hyperplasia.

In our estimate, with the present method, if adequate technical quality is maintained, the anatomic structures properly identified and diagnostic criteria strictly observed, lymph node enlargements in the abdomen can be diagnosed echographically with no more than 10 per cent (and most likely less) *false negative* results. The lesser pelvis was not included in this study. We are continuing work in that area and on the effects of treatment or lymphangiography on echographic representation of lymph nodes.

Under the same conditions, *false positive* results will be obtained in less than 5 per cent of the cases.

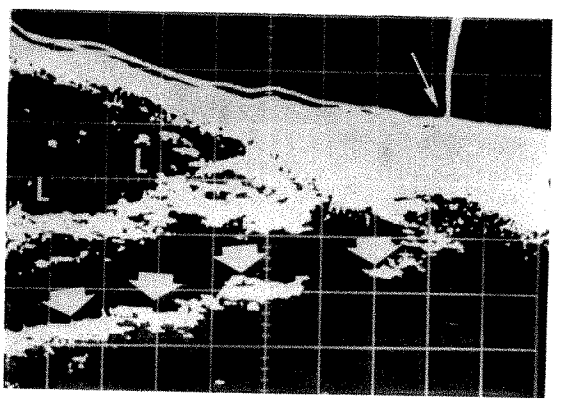


FIG. 4. Midline sagittal scan in an elderly patient without lymphoma. Our longitudinal scan figures are placed so that the patient's front is up and the caudal end of the body to the reader's right. The marker at the top (white arrow) shows how the reference point, the iliac crest, is located on the scan image. The anterior vertebral border together with the posterior wall of the aorta forms a well-defined echo line (multiple white arrows), the black strip just above this is the aorta; in this case, it is highly bumpy and irregular because of atheromatous changes; it can be seen to end at the iliac crest level which corresponds roughly to the aortic bifurcation. The edge of the left lobe of the liver (L) can be seen protruding down into the abdomen on the left of the figure above the aorta. Note absence of separate pre-aortic masses.

DISCUSSION

SELECTION OF SCANNING TECHNIQUE

Of the possible approaches, the anteroposterior transverse section was selected as least subject to error in presentation. The lateral recumbent position was not chosen because it caused organ displacement and abdominal sag toward the dependent side, particularly in obese patients, making comparison with normals impossible. Displacement of normal structures could not be evaluated if the patient was moved into different positions during the course of scanning. Scanning of the prevertebral area from the back with the patient prone was unsatisfactory with our equipment because of impedance of the sound beam by the relatively thick muscle and reverberations by bone structures.

In addition, sagittal plane longitudinal scans were obtained in the midline and at 3 and 6 cm. to each side of it. The sagittal scans were quite helpful, particularly the midline section. We consider these scans essential in that some lesions would be overlooked when relying on only the transverse sections (Fig. 4).

Demonstration of a mass or masses on 2 scans obtained at right angles to each other was valuable both as an agent of detection and of positive confirmation in a manner similar to the anteroposterior and lateral projections in roentgenology (Fig. 5, *A* and *B*).

Scanning in this manner, we felt that masses greater than 1.5 cm. could be detected. Once masses were observed or suspected, scans in between the standard levels occasionally contributed to the diagnosis.

The iliac crest was chosen as the reference point because it could readily be identified on abdominal roentgenograms in any projection and therefore was a valid point for measurement in roentgen correlation.

SOURCES OF ERROR IN INTERPRETATION

A. *Equipment.* Display errors are due to the beam width, the inherent limitation of depth resolution related to wave length, linkage slack, and blossoming of the oscilloscope storage image. Considering these errors, we believe that with present equipment, masses over 1.5 cm. in diameter can be detected reliably, if located in the retroperitoneal area in front of the spine, psoas muscles and kidneys.

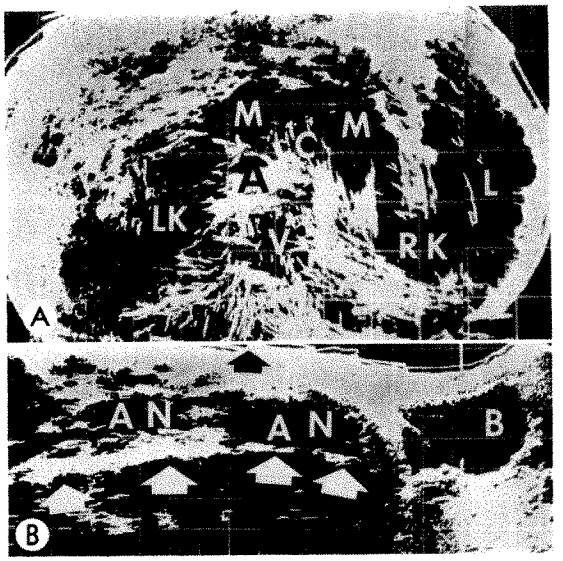


FIG. 5. (*A*) Sonolucent lymph node mass (M) in front and to the right of the spine. The "draped" arrangement of the mass over the anterior contour of the spine is fairly typical. V—vertebral body, L—right lobe of liver, RK—posterior contour of right kidney, LK—left kidney, A—aorta, C—vena cava. (*B*) The sagittal midline section confirms the lymph node masses seen in Figure 5*A*. In addition, they can be seen to extend into the pelvis on this scan. The single black arrow marks the reference point, the iliac crest. White arrows—anterior contour of vertebral bodies, AN—lower abdominal aorta with closely surrounding lymph node masses, extending below the level of the aortic bifurcation. B—urinary bladder.

B. *Equipment Settings.* The *intensity* of the oscilloscope should be set to print in storage mode with a small well-defined dot and should remain constant throughout the examination. The *gain* should be adequate to penetrate all the structures one desires to view. The *sensitivity* must be high enough to give good anatomic outline of the spine, liver, spleen and prevertebral structures, yet not so high that too many return echoes are recorded, confusing organ

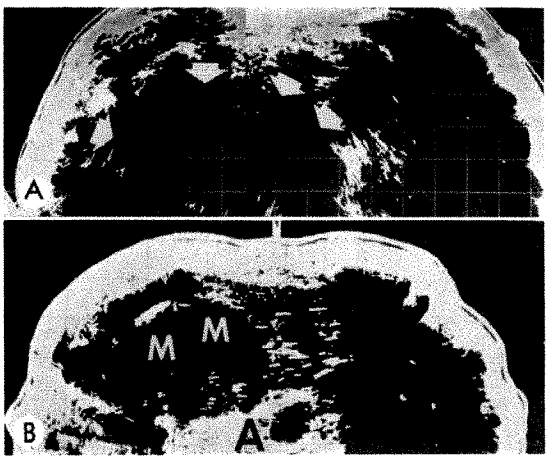


FIG. 6. (*A*) This cross section composite taken at 15 cm. above the iliac crest (high in the abdomen) demonstrates a large anechoic area (white arrows) which may or may not be a mass. In this case the appearance is due to gas shadows and scattering by multiple bowel loops. Note the absence of the entire spine outline and retroperitoneal echoes. Even if a mass were present, no reliable opinion could be given, since through transmission of sound is not shown. If this were a solid mass, increase in sensitivity or gain settings would eventually show the posterior wall of the mass—or structures beyond it. (*B*) This section was taken at the same level as that in Figure 6*A* but in a different patient, demonstrating a large sonolucent mass (M) behind the stomach and adjacent to the left lobe of the liver. The mass was removed at surgery and identified as a leiomyosarcoma. Note the prominent outline of the spine and retroperitoneal echoes (A) distinguishing it from the false mass seen in Figure 6*A*.

Masses of different histologic nature may differ in their ability to transmit sound. Nevertheless, for reliable diagnosis, an effort has to be made to separate acoustic shadows (anechoic areas) from sonolucent (sound transmitting) masses by proving the return of echoes from beyond the lesion.

outlines. Once a mass is detected, increasing the sensitivity by increments during successive scans over the same area can give an idea of whether the structure examined is homogeneous in density (and therefore has no internal interfaces of different acoustic impedance), or whether it has differences in internal structure. On each level examined, scans are obtained routinely at 3 different sensitivities. Persistent demonstration of a mass at increasing sensitivity settings (below the sensitivity setting level at which known normal structures start filling in with echoes) confirms its real nature and excludes some types of artifacts (Fig. 7, *A* and *B*). At the present time, the type of echo cannot be correlated with histologic findings in all cases. Additional experience may make it possible to differentiate many biologic characteristics of tumors by phase change detection or echo patterns.

C. *Interpretation of Findings.* The major physiologic factors which interfere with adequate depiction of anatomic structures and lesions are intestinal gas and collections of multiple bowel loops. Air or gas interposed between the transducer and target organ reflect or disperse the sound waves, thus preventing the visualization of the target organs. The large black area of no echo return may be erroneously interpreted as a sonolucent mass (Fig. 6*A*). It can be differentiated from true sonolucent masses which transmit sound by ensuring that structures distal to the "mass" are visualized (Fig. 6*B*). Abdominal scan information can be considered reliable when the vertebral body is well outlined,

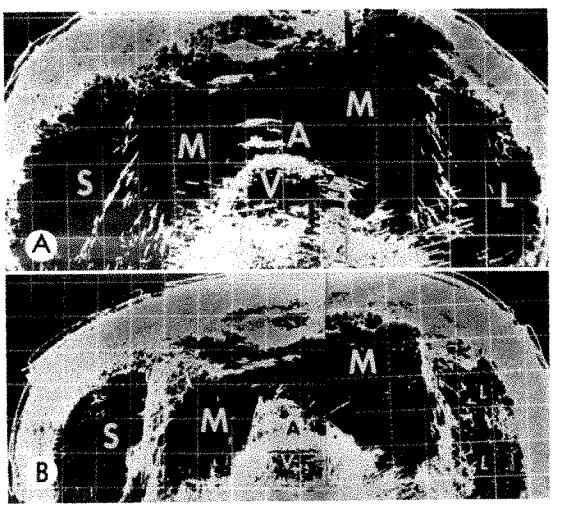


FIG. 7. Cross sections of a lymphoma patient at the same level (6 cm. above the iliac crest), but taken at different sensitivity settings. (*A*) Vague outline of the para-aortic lymph node masses (M). (*B*) Good delineation of these masses at higher sensitivities. The "dumbbell" shape of these masses in cross section is also characteristic of lymph node masses. S—spleen, L—lower part of right lobe of liver, V—vertebral body, A—aorta.

proving that the sound beam has traversed all structures between the skin and the spine. Therefore, any sonolucent areas transmitting sound to structures beyond can be differentiated from gas collections in the bowel which cast acoustic shadows (Fig. 6, *A* and *B*).

Sound reflection by bone causes multiple reverberations which sometimes prevent true representation of the echo characteristics of underlying structures.

If no attempt is made to stop the patient's respiration during each scanning pass, the echoes represent the average size and position of moveable intra-abdominal organs and some definition will be lost, particularly in the upper abdomen.

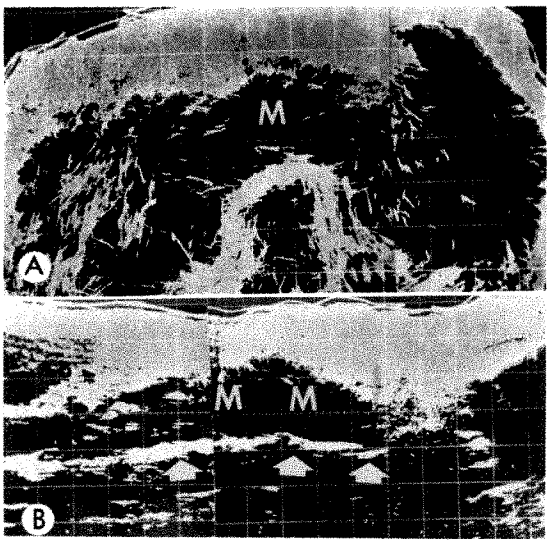


Fig. 8. (*A*) Aortic contour completely obliterated in this patient with lymphosarcoma, with a large sonolucent mass (M) surrounding the aorta. The cross section was taken in mid abdomen with the lower border of the liver still appearing on the right and the kidney outline seen on the left. Again note the well-outlined vertebral body and the "draped" arrangement of the masses in front of the spine. (*B*) Longitudinal midline scan. Demonstration of extent of the lymph node masses (M)—a fact not readily appreciated with the cross section scan alone. White arrows point to anterior contour of vertebral bodies. Note how the aortic contour disappears in the lymph node masses.

DIAGNOSIS

Enlarged lymphoma lymph nodes tend to be "sonolucent," as are most other prevertebral masses if they have a relatively homogeneous internal structure.

Masses of physically homogeneous structure—enlarged lymph nodes, some sarcomas, fluid collections, aneurysms and cysts appear as abnormal sonolucent areas sometimes displacing normal structures. Their shape, location, outline characteristics and associated findings permit differentiation in many instances. Irregular infiltrating lesions cause a grossly irregular, spotty echo pattern with severe loss of normal organ outline echos, if such organs are invaded. Localized noninfiltrating masses, even if malignant, when localized in between other normal structures can be outlined well and show evidence of apparent compression of adjacent organs.

The diagnosis of para-aortic lymph node enlargement or infiltration of para-aortic tissues is made if sonolucent masses can be identified directly on the echogram (Fig. 7*B*; and 10) or when the normal aortic contour is obliterated by the surrounding masses (Fig. 8, *A* and *B*). Obliteration of the aortic contour, while the vertebral outline is still preserved, has proven to be a helpful diagnostic criterion. Because this in some respects is similar to the roentgen silhouette sign, we have termed this phenomenon the aortic "echo silhouette sign." This "echo silhouette sign" also applies to infiltration closely adjacent to and into other organs which normally have a well-defined border.

However, in patients with calcified or otherwise unusually dense aortic walls, para-aortic lymph node masses may not produce this sign (Fig. 9, *A* and *B*).

Characteristic anatomic patterns of abdominal lymph node enlargement are recognized in many cases with increasing experience. These patterns include: (a) Large roundish masses (Fig. 3, *A* and *B*; and 10); (b) a mantle-like, "draped" continuous plaque of lymph nodes around and anterior to the aorta (Fig. 5, *A* and *B*; and 8, *A* and *B*); (c) a dumbbell-like grouping (Fig. 7, *A* and *B*); and lastly, (d) scattered multiple separated masses (Fig. 9*B*; and 10).

Hepatic and particularly splenic enlargements can be identified by their typically

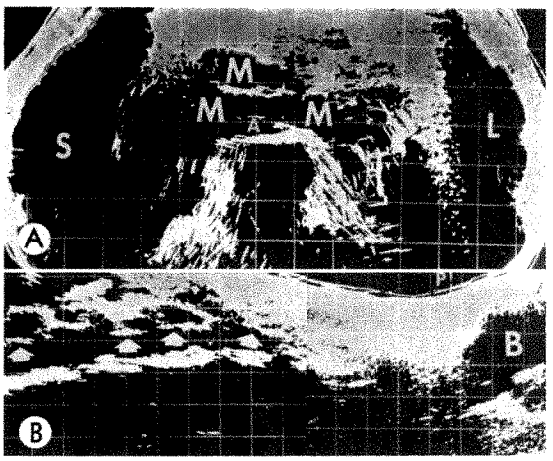


FIG. 9. (*A*) Large group of sonolucent lymph nodes (M) ahead and to either side of the aorta (A) in this cross section illustration. Note that in this case some of the lymph node masses are not in direct contact with the aorta. S—spleen, markedly enlarged; L—enlarged right lobe of the liver. (*B*) Sagittal midline section in the same patient demonstrates the individual lymph node masses seen just in front of the aorta (white arrows point to anterior wall of aorta); heavy zone of echoes behind aorta represents anterior contour of vertebral bodies; B—urinary bladder, marker P—upper edge of pubic symphysis.

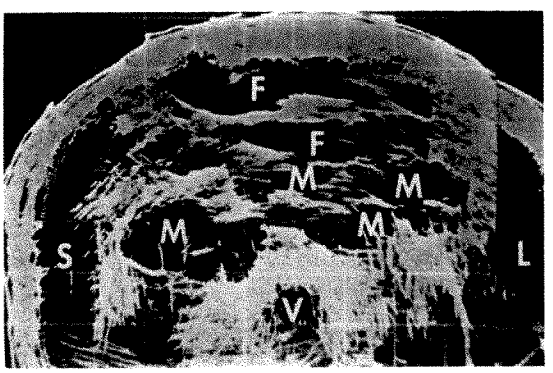


FIG. 10. Twelve year old girl with known abdominal lymphosarcoma. Transverse section 6 cm. above iliac crest. M—multiple lymph node masses in the para-aortic and mesenteric area, L—right lobe of enlarged liver, S—lower edge of enlarged spleen, V—vertebral body, F—probably ascitic fluid. Sonolucent areas "L" and "S" are also in many respects suggestive of peritoneal fluid, which characteristically accumulates, at least in part, in the flanks in this manner. It can be differentiated in most cases from liver and spleen by following the contour of these organs downward on successive scans and determining the downward extent of liver and spleen on longitudinal sections.

curved posteromedial contour (preserved even in marked enlargement), and by obvious characteristic organ compression toward the midline in the case of enlargement of these two structures (Fig. 11). If lymph node masses are very large, they can also cause this compressed tissue effect.

The presence of ascites improves the subjects acoustic transmission characteristics. The fluid causes sonolucent areas surrounding normal or abnormal structures. These sonolucent areas also can be erroneously interpreted as masses if careful analysis of the same anatomic area at selected sensitivity settings is not performed.[6] If the ascitic fluid is free, it can often be identified as a sonolucent layer over the surface of the liver and in elongated collections in the flanks.

CONCLUSION

This study indicates that ultrasound "B" mode contact scanning is useful in the detection, delineation of extent, and diagnosis of organ of origin in many cases of retroperitoneal masses. Lymphomatous enlarged lymph nodes in para-aortic, subhepatic, retrogastric and other abdominal areas can be identified fairly readily if they are more than 1.5 cm. in diameter.

If a satisfactory scan is obtained, such lymph nodes can be detected more reliably

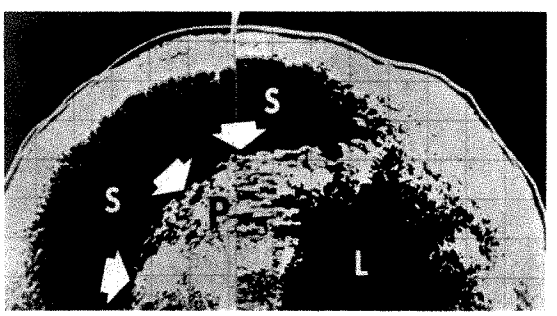


FIG. 11. The huge spleen (S) in this patient with lymphosarcoma preserves the smooth medial border (white arrows) while depressing tissues toward the midline. The liver (L) occupies the right half portion of the photograph. Note multiple echoes from compressed prevertebral structures (P), but without evidence of prevertebral lymph node enlargement.

by echography than by roentgenographic gastrointestinal and urographic examinations. Of course, the latter have the advantage of occasionally showing intrinsic disease.

After a few weeks training, technicians are able to obtain satisfactory scans in most patients.

Echography permits demonstration of lymph node enlargements in areas not filled by conventional lymphangiography due to the anatomic distribution of lymph drainage channels, *e.g.*, mesenteric, retrogastric and subhepatic lymph nodes.

We have encountered difficulties in evaluating the lymph nodes in the lesser pelvis. We believe, however, that with improved scanning techniques and increasing knowledge of echographic anatomy, lymph node masses in this area will become accessible to echographic diagnosis.[7]

In those lymphoma patients in whom there is anterior displacement of the stomach on upper gastrointestinal series, and who have an enlarged spleen, echography permits the exclusion or confirmation of enlarged retroperitoneal lymph nodes causing such displacement, a differentiation which is very hard to make by any other means, since the spleen alone may also displace the stomach anteriorly.

Changes in the size of organs or masses can be observed by serial echography following treatment.

Aortic aneurysms can cause displacement of the ureters and parts of the gastrointestinal tract. Echography permits diagnostic separation of aneurysm from lymph node enlargement (in addition to being a reliable procedure for detection of aortic aneurysm).[2]

SUMMARY

The use of ultrasound "B" mode scanning in the diagnosis of enlarged retroperitoneal lymph nodes and other retroperitoneal masses was studied involving analysis of over 300 patients and controls. This method was found to be a useful procedure. Technical features and limitations, details of interpretation as well as diagnostic criteria are discussed.

At the present stage of development, echographic study of lymphoma patients will outline almost all enlarged lymph node groups in the abdominal area and will add some areas not seen by conventional roentgen examination. In those patients who are considered for curative radiation therapy, both lymphangiography and echography are desirable in addition to other roentgen studies.

Atis K. Freimanis, M.D.
Department of Radiology
Ohio State University
410 West 10th Avenue
Columbus, Ohio 43210

Appreciation is expressed to Sidney W. Nelson, M.D., Chairman, Department of Radiology, Ohio State University for approval and departmental support; to Frank Batley, M.D., Director of Radiation Therapy for support and space; to Bertha Bouroncle, M.D., Division of Hematology and Medical Oncology for cooperation in the study of patients; to Mr. Dale Ensminger, Sonics Engineering Consultant, Battelle Memorial Institute; and to Mrs. Martha Crawford for secretarial and clerical assistance.

REFERENCES

1. Blitz, J. Fundamentals of Ultrasonics. Second edition. Plenum Press, New York, 1967.
2. Goldberg, B. B., Ostrum, B. J., and Isard, H. J. Ultrasonic aortography. *J.A.M.A.*, 1966, *198*, 353–358.
3. Grossman, C. C. Editor. Proceedings of the First International Conference. Plenum Press, New York, 1966.
4. Holmes, J. H. Present status of ultrasonic diagnostic techniques in internal medicine. *Ultrasonics*, 1967, *5*, 60–66.
5. Howry, D. H. Brief atlas of diagnostic ultrasonic radiologic results. *Radiol. Clin. North America*, 1965, *3*, 433–452.
6. Lehman, J. S. Ultrasound in diagnosis of hepatobiliary disease. *Radiol. Clin. North America*, 1966, *4*, 605–623.
7. Thompson, H. E., Holmes, J. H., Gottesfeld, K. R., and Taylor, E. S. Ultrasound as diagnostic aid in diseases of pelvis. *Am. J. Obst. & Gynec.*, 1967, *98*, 472–481.

A MODIFIED TECHNIQUE OF ULTRASONOGRAPHY FOR THE DETECTION AND DIFFERENTIAL DIAGNOSIS OF BREAST LESIONS*

By FRANK H. DELAND†
BALTIMORE, MARYLAND

TWO dimensional ultrasonography offers considerable potential as a diagnostic technique for the visualization of soft tissue structures. Dussik *et al.*[2] in 1947 reported one of the first diagnostic applications of ultrasound to biologic tissues and in 1950, Wild[6] concluded from his investigations that information obtained by ultrasonic examination could be of value in medicine. By 1952 instruments had been developed which were capable of producing a pictorial cross section of anatomic structures.[4,7] This two dimensional technique was obtained from a consecutive series of one dimensional sound reflections integrated to form a composite picture. Although considerable advances in instrumentation have been made since the original work in two dimensional ultrasonography, resolution of presently available transducers is limited since compromises must be made in the choice of crystal size and ultrasonic wave length. The purpose of this study was to investigate methods of improving resolution. Modifications of equipment were evaluated by scanning palpable breast tumors.

METHOD

PRINCIPLE

Pulsed ultrasonic radiation from a focused transducer travels through soft tissues with velocities of approximately 1,470 to 1,570 meters per second. The detected sound waves reflected from interfaces are electronically amplified and displayed on a cathode ray tube at the positions which correspond to the depths of the interfaces and displacements of the beam. Fluid with an acoustic impedance similar to that of tissue is used to couple the transducer and the tissue surface. As the transducer moves across the anatomic area, a series of one dimensional sound reflections are recorded, forming a two dimensional picture. This cross section representation of the tissue is displayed on an oscilloscope tube and is recorded on Polaroid film.

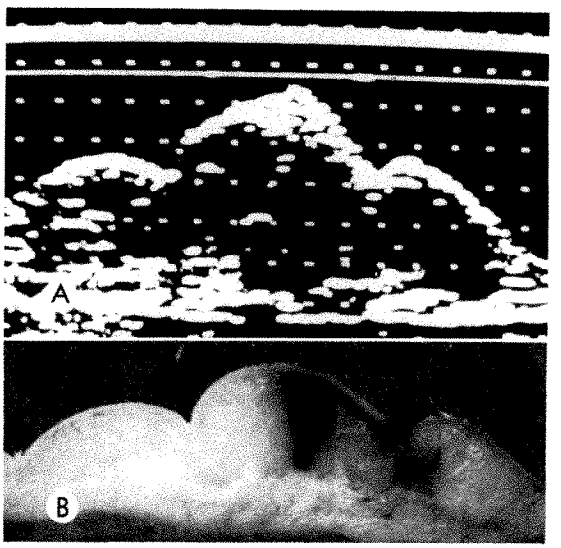


FIG. 1. (*A*) Breast scan made with 0.5 inch transducer. (*B*) Cross section of breast corresponding to scan.

EQUIPMENT AND MODIFICATIONS

These studies were performed with a transistorized ultrasonic transmitter-receiver designed specifically for medical purposes. All procedures were carried out at a frequency of 2.25 million cycles per second (2.25 Mc.). A transducer with a 0.5 inch crystal was used in the preliminary investigations. Figure 1*A* shows a breast

* From the Division of Nuclear Medicine, The Johns Hopkins Medical Institutions, Baltimore, Maryland.
Supported by a grant from the American Cancer Society, Florida Division.
† Formerly: Director of Laboratory Medicine, Lakeland General Hospital, Lakeland, Florida.

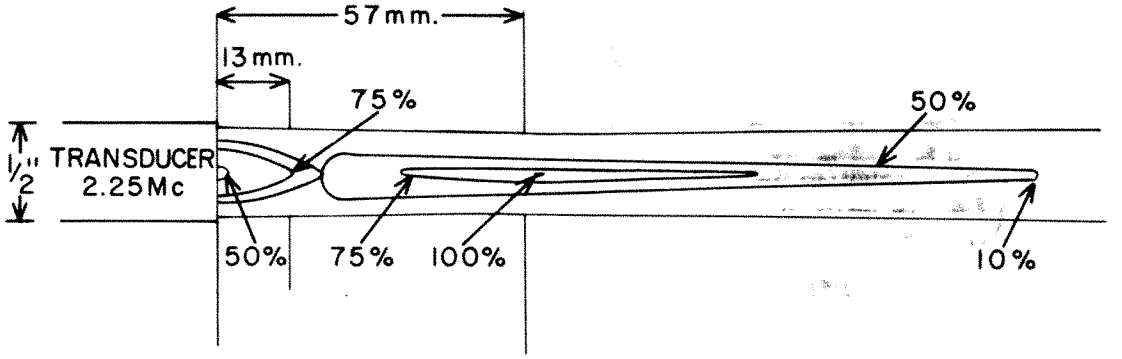


FIG. 2. An intensity plot of a 0.5 inch transducer (2.25 Mc.).

scan made with this transducer, and Figure 1*B* the corresponding anatomic section. The reflected waves from the minute interfaces were recorded as coarse "blips." Although the transducer was operating in the tissue depth range where the beam size approximated the crystal size (*i.e.*, there was no divergence of the beam), the tumor was not well differentiated from the surrounding tissue. The resolution was not adequate for detecting fine differences in tissue structures.

Lateral resolution is directly related to beam diameter and divergence. As the diameter becomes smaller, resolution improves but divergence occurs closer to the crystal face, diminishing resolution. The penetrating power of the beam is inversely related to its diameter. To obtain the narrow beam of a small crystal and retain the power of a large crystal, the 0.5 inch transducer was collimated to restrict the diameter of the ultrasonic beam. The collimator was made of 3/8 inch thick cork with a central aperture of 6 mm. and was affixed to the face of the crystal. This eliminated ultrasonic wave emission from the periphery of the crystal and restricted the beam to power intensities of 50 per cent or greater (Fig. 2). Figure 3*A* demonstrates a scan made with this device. The recorded signals were finer and the scan had better resolution than without collimation (Fig. 3*B*), but marked reverberations were present at the junction of the cork and crystal face. This is seen as a broad horizontal band of signals above the tissue.

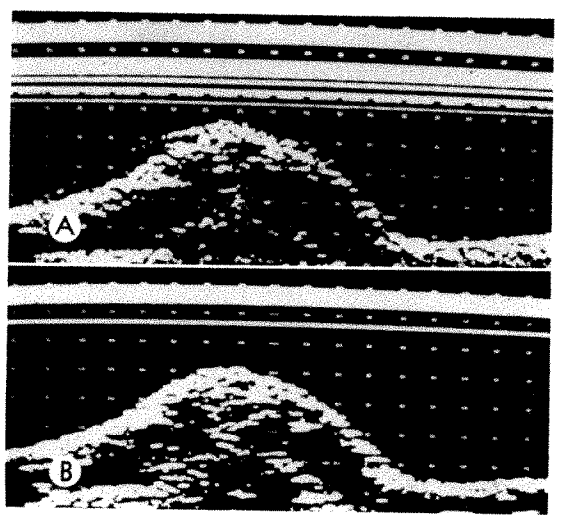
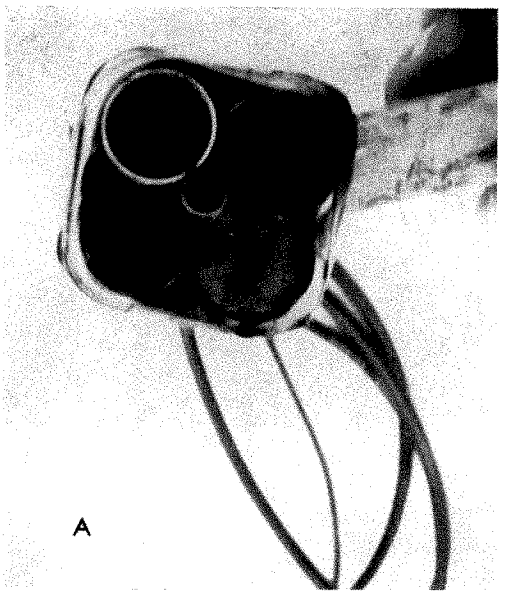


FIG. 3. (*A*) Breast scan made with a collimated 0.5 inch transducer. (*B*) Breast scan made without collimation.

Better lateral resolution is obtained with a narrow beam, but the detection of reflected sound waves is limited by the small diameter of the crystal. Increased information can be obtained by using separate receiving crystals with diameters larger than that of the emitter. A 0.25 inch transducer was selected for the emitter and four 0.5 inch transducers for the receivers (Fig. 4*A*). The 0.5 inch units were grouped around the emitter so that the center line of each intersected at a point 3.5 cm. in front of the emitter-transducer (Fig. 4*B*). This focal point was chosen since there is minimal divergence of the ultrasonic beam at this distance.

The surface area of the four 0.5 inch



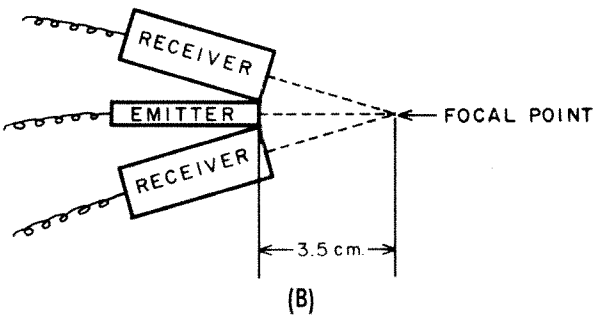


Fig. 4. (*A*) Array of transducers. (*B*) Schematic diagram showing alignment of transducers.

crystals is 0.8 square inches (sixteen times the single 0.25 inch unit) and their relationship to a returning sound front from a point interface is shown in Figure 5. The number of detected echoes was markedly increased, making it possible to electronically reject weak and spurious echoes and to reduce the electronic amplification to less than half of that required by a single transducer. The reflected echoes displayed on the cathode ray tube were finer with the multiple transducers than with a single unit.

MODIFICATION OF WATER COUPLING

The transducers were coupled to the skin by immersion in a plastic sac filled with degassed, warm water, containing 1 per cent sodium chloride. An adhesive surgical drape* suspended on a framework formed the sac, and an opening was made in the bottom so that the breast could be in direct contact with the water coupler (Fig. 6). The drape was then placed around the breast and molded to the skin of the chest to form a watertight seal. The sac was filled to a level 2 to 3 cm. above the breast, and the transducers were lowered to within 1 cm. of the breast surface. This type of

* Johnson and Johnson Company New Brunswick N. J.

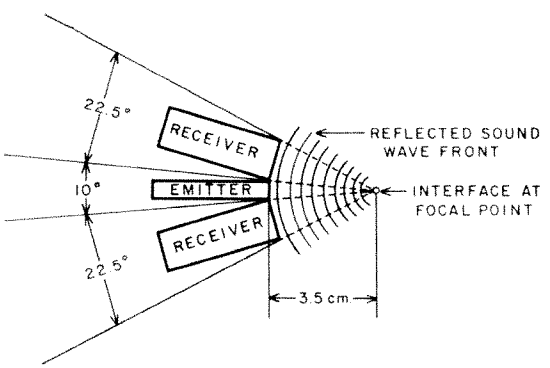


Fig. 5. Schematic diagram showing relationship of reflected sound waves to the array of transducers.

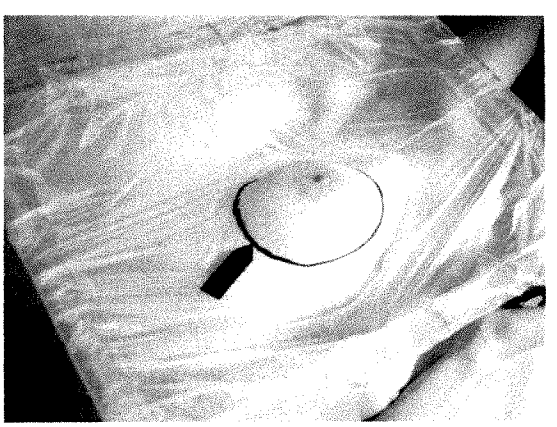


Fig. 6. The margin of the opening is outlined (arrow). The breast is in direct contact with the water.

water bath eliminated a plastic interface between the tissue and the transducer and also prevented physical distortion of the breast.

PROCEDURE

Sixty-nine female patients from the Surgical Service of the Lakeland General Hospital, Lakeland, Florida, were selected for this investigation. Each case had been admitted for biopsy of a palpable breast mass. The patients were examined in a supine position, with the shoulder and chest elevated, placing the breast in a horizontal plane. Transverse scans of the breast were made at 0.5 cm. intervals in the area of the lesion. The scans were made with both the single 0.25 inch transducer and the array of transducers. The surgical biopsies were processed and immediate correlation was made between the preoperative diagnosis from the ultrasonic scan and the postoperative histologic diagnosis.

RESULTS

The skin of the normal breast was identified as a continuous band of reflected sound, 2–3 mm. thick, conforming to the contour of the breast (Fig. 7*A*). Scattered echoes were found within the nipple (Fig. 7*B*). The fatty tissue was represented by a homogeneous mass of small echoes, which occurred at the multifibrous septa (Fig. 7*A*). Glandular tissue, although usually obscured by the fat, was visualized as linear bands void of echoes.

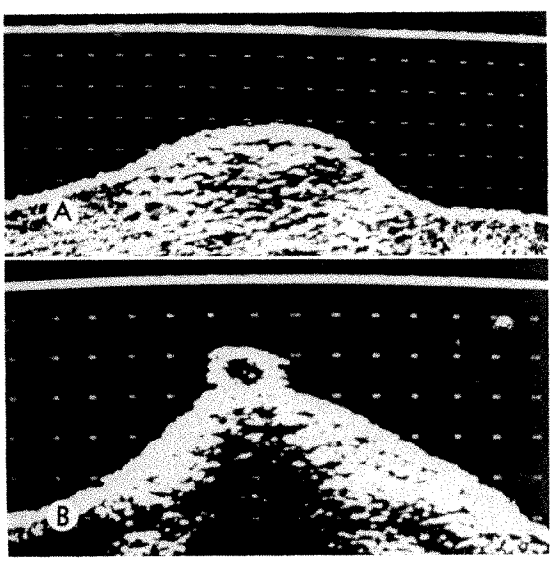


Fig. 7. (*A*) Ultrasonic scan of normal breast. (*B*) Scan of normal breast including nipple.

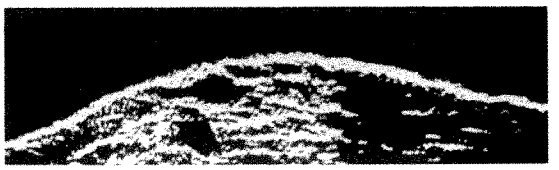


Fig. 8. Scan of unilocular cyst of the breast (arrow).

Benign lesions did not reflect the sound waves and appeared homogeneous except in a few instances. The interface boundary between the margin of the tumor and the rounding breast tissue was well delineated and was either smooth or slightly irregular. The borders of cysts were smooth, and there were no echoes from contents. Figure 8 demonstrates a scan of a unilocular cyst. Fibroadenomata appeared similar except that the borders were slightly irregular (Fig. 9). The margins of a fibrocystic lesion were generally irregular and the tissue appeared homogeneous, although in some cases a few echoes were seen within the lesion (Fig. 10, *A* and *B*).

Malignant tumors were well demarcated and the borders were irregular and often appeared serrated. There were usually numerous echoes recorded within the neoplasm, probably representing fibrous bands, areas of cystic degeneration, and calcium deposits. Scans of scirrhous adenocarcinoma of the breast are shown in Figure 11, *A* and *B*. In neoplasms that were more



Fig. 9. Scan of a fibroadenoma of the breast.

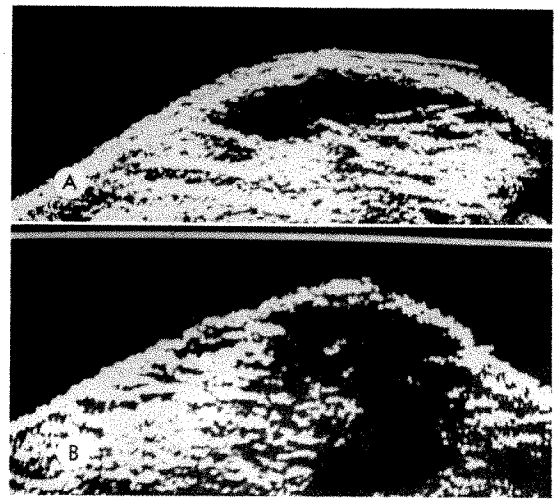


FIG. 10. (*A*) Scan of fibrocystic disease of the breast. (*B*) Scan of fibrocystic disease of the breast showing a few echoes in the lesion.

homogeneous, such as medullary adenocarcinoma, the margins were regular, and there were no echoes within the lesion (Fig. 12, *A* and *B*).

In this series of 69 patients there were 19 malignant and 50 benign breast lesions (Table 1). The accuracy in diagnosis of benign tumors was essentially the same with both systems (single or multiple transducers). Those cases which were misdiagnosed demonstrated echoes within the lesion. Macrocysts were present in these lesions, and presumably caused the reflections.

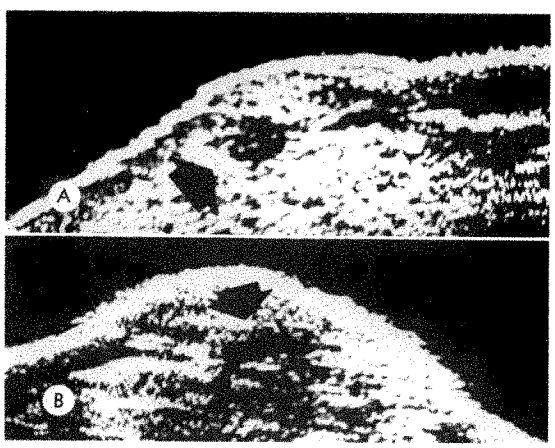


FIG. 11. (*A* and *B*) Breast scans of 2 patients with scirrhous adenocarcinoma (arrows).

Fifteen of the 16 cases of scirrhous adenocarcinoma were correctly diagnosed preoperatively with the multiple transducer system, whereas only 9 of these 16 cases were correctly diagnosed with a single probe. The 3 cases of medullary adenocarcinoma were misdiagnosed with both systems.

DISCUSSION

Several methods have been developed to improve the resolution of ultrasonic transducers. One of these is compound scanning, a combination of linear and sector motion of the transducer. Thurstone and McKinney[2] developed a point focused transducer by using geometric surfaces to reflect and focus the ultrasonic beam. Only those echoes from the focal point were detected and recorded point by point rather than line by line. The transducer is moved in two directions to obtain a two dimensional image. A similar geometric arrangement was reported by Hertz.[3] Denier van der Gon *et al.*[1] constructed a probe composed of a central emitting crystal surrounded by a ring shaped receiver. From their diagram the surface area of the receiving crystal appears to be four times that of the emitter. Their results are described as being com-

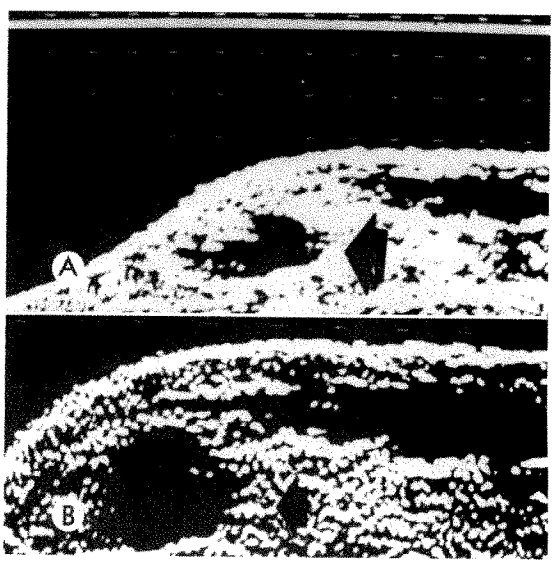


FIG. 12. (*A* and *B*) Breast scans of 2 patients with medullary adenocarcinoma (arrows).

TABLE I

SUMMARY OF CASES

	Histologic Diagnosis	Ultrasonic Diagnosis			
		Transducer Array		Single Transducer	
		Benign	Malignant	Benign	Malignant
Benign Lesions (50 Cases)	Fibrocystic Disease (38)	36	2	36	2
	Fibroadenoma (10)	10		10	
	Papillomatosis (1)	1		1	
	Lobular Hyperplasia (1)	1			1
	Total	48	2	47	3
	Per Cent	96		94	
Malignant Lesions (19 Cases)	Scirrhous Adenocarcinoma (16)	1	15	7	9
	Medullary Adenocarcinoma (3)	3		3	
	Total	4	15	10	9
	Per Cent		79		46

parable to those of a single probe in combination with a compound scanning movement.

The diameter of the transducers used in medical diagnostic instruments is considerably larger than the wave length emitted, and the beam size approximates crystal size (Fig. 2). These factors limit the resolution of interfaces perpendicular to the beam. For example, metal bodies 1 mm. in diameter were resolved with a 0.5 inch transducer (2.25 Mc.) as linear structures 4–6 times that length. Better lateral resolution can be obtained with a small beam, but the information received (number of detected echoes) is limited by the small surface area of the crystal and the power depletion with tissue penetration. Echoes detected by a single transducer must be reflected from interfaces nearly perpendicular to the path of the beam. For example, at a point 3.5 cm. in front of a 0.5 inch transducer, the angle subtended is about 20°, and with a 0.25 inch crystal is only 10°. Interfaces at angles greater than 10° and 5°, respectively, to the perpendicular plane will reflect out of the range of the crystal face.

The array of transducers used in this study increased the angle subtended to 55°. Interfaces at angles up to 25.7° from the perpendicular to the beam are detected. The larger subtended angle and receiving surface of the crystals markedly increased the number of detected echoes, providing scans of improved diagnostic quality. The signals recorded on the oscilloscope were finer and the entire periphery of tumors was outlined.

Figure 13*A* shows a cross section of a breast specimen through the lesion (scirrhous adenocarcinoma). Figures 13, *B* and *C* are preoperative scans of this breast through the carcinoma. Figures 13, *D* and *E* represent postoperative scans of the amputated breast. The scans obtained with the transducer array gave better definition of the lesion.

Sound waves that intersect the surface of the receiving crystal are not necessarily from an interface that is approximately perpendicular to the beam. An ultrasonic impulse can be reflected from several surfaces, strike the receiving crystal, and the last interface may have no relationship to the path of the emitted beam. The intensity of multireflected echoes is diminished. The returning signal with the bank of transducers was sufficiently intense that the rejection level for weaker signals was

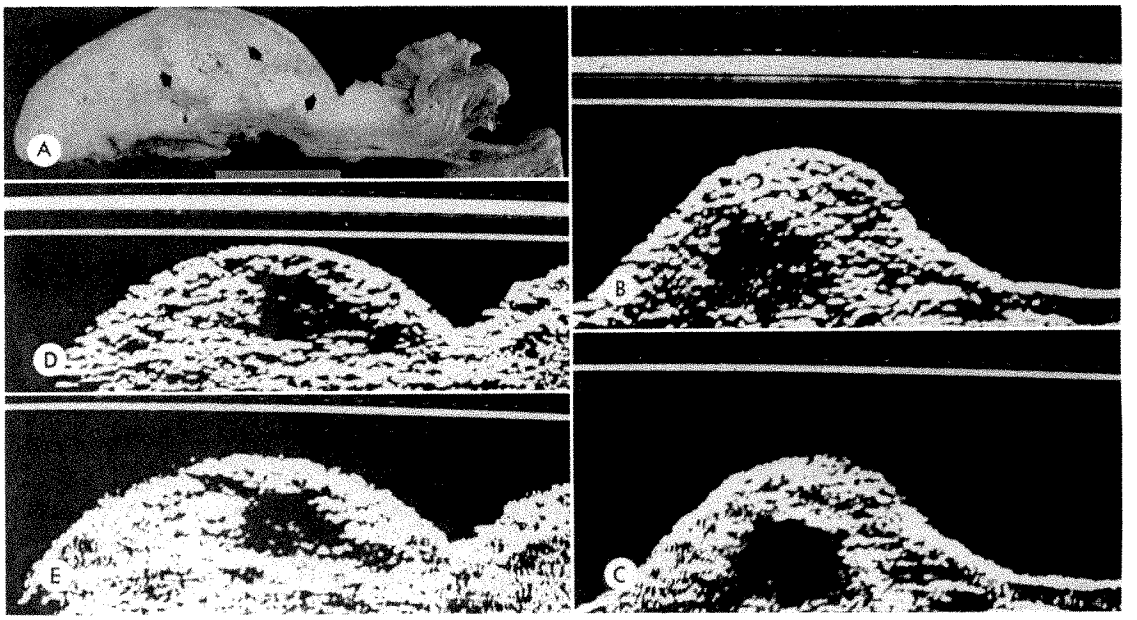


FIG. 13. (*A*) Cross section of a breast specimen with scirrhous adenocarcinoma. (*B*) Preoperative scan of breast lesion with single transducer. (*C*) Preoperative scan of breast lesion with transducer array. (*D*) Postoperative scan of amputated breast with single transducer. (*E*) Postoperative scan of amputated breast with transducer array.

2–3 times higher than with the single transducer. It was necessary to record 80 per cent of the signal to obtain a satisfactory image from a single transducer. Only the stronger signals (40 per cent) were recorded with the bank of transducers, the remainder were rejected (60 per cent).

SUMMARY

1. Modifications of the ultrasonic scanning head are described.

2. Separation of the emitting and receiving crystals provided a more intense reflected signal and improved resolution.

3. Modification of the water bag coupler eliminated the plastic interface and prevented distortion of soft tissues from pressure.

4. The results of the investigation of breast lesions with these modifications are reported.

Department of Radiological Science
615 North Wolfe Street
Baltimore, Maryland 21205

REFERENCES

1. DENIER VAN DER GON, J. J., MOLIN, C. E., and DE VLIEGER, M. Comparison of scan techniques in two-dimensional echo-encephalography. Diagnostic Ultrasound. Proceedings of the First International Conference. Plenum Press, New York, 1966.

2. DUSSIK, K. T., DUSSIK, F., and WYT, L. Auf dem Wege zur Hyperphonographie des Gehirnes. *Wien. med. Wchnschr.*, 1947, *97*, 425–429.

3. HERTZ, C. H. Ultrasonic heart investigations. *Med. Electronic & Biol. Eng.*, 1965, *2*, 39–45.

4. HOWRY, D. H., and BLISS, W. R. Ultrasonic visualization of soft tissue structures of body. *J. Lab. & Clin. Med.*, 1952, *40*, 579–592.

5. THURSTONE, F. L., and MCKINNEY, W. M. Focused transducer arrays in ultrasonic scanning system for biologic tissue. Diagnostic Ultrasound. Proceedings of the First International Conference. Plenum Press, New York, 1966.

6. WILD, J. J. Use of ultrasonic pulses for measurement of biologic tissues and detection of tissue density changes. *Surgery*, 1950, *27*, 183–188.

7. WILD, J. J., and REID, J. M. Further pilot echographic studies on histologic structures of tumors of living intact human breast. *Am. J. Path.*, 1952, *28*, 839–861.

VOL. 105, NO. 2

THE AMERICAN JOURNAL OF ROENTGENOLOGY RADIUM THERAPY AND NUCLEAR MEDICINE

Editor: TRAIAN LEUCUTIA, M.D.

Assistant to the Editor: KENNETH L. KRABBENHOFT, M.D.

Associate Editors: HARRY HAUSER, M.D., RUSSELL H. MORGAN, M.D., EDWARD B. D. NEUHAUSER, M.D.

Consulting Editorial Board: See front cover.

Published by: CHARLES C THOMAS, Publisher, 301–327 East Lawrence Avenue, Springfield, Illinois 62703.

Issued monthly. Annual subscription: United States, Mexico, Cuba, Central and South America, and Canada $20.00; other countries, $22.00. Current single numbers, $2.00. Advertising rates submitted on application. Editorial office, 401 Professional Building, Detroit, Michigan 48201. Office of publication, 301–327 East Lawrence Avenue, Springfield, Illinois 62703. Information of interest to authors and readers will be found on page ii.

AMERICAN ROENTGEN RAY SOCIETY

President: S. W. Brown, Augusta, Ga.; *President-Elect:* J. C. Cook, Detroit, Mich.; *1st Vice-President:* S. F. Ochsner, New Orleans, La.; *2nd Vice-President:* Herbert M. Stauffer, Philadelphia, Pa.; *Secretary:* T. F. Leigh, Emory University Clinic, Atlanta, Ga. 30322; *Treasurer:* C. B. Holman, Mayo Clinic, Rochester, Minn. 55901.

Executive Council: S. W. Brown, J. C. Cook, S. F. Ochsner, T. F. Leigh, C. B. Holman, T. M. Fullenlove, W. N. Hanafee, J. F. Roach, C. M. Nice, Jr., E. F. Lang, H. O. Peterson, C. A. Stevenson, C. A. Good, T. Leucutia, R. M. Scott, S. W. Nelson, R. L. Tondreau, W. B. Seaman, E. F. Van Epps, Chairman, Duke Univ., Durham, N. C., 27706.

Program Committee: T. F. Leigh, J. F. Roach, T. Leucutia, E. F. Lang, H. O. Peterson, W. N. Hanafee, S. W. Brown, E. F. Van Epps, J. C. Cook, Chairman, LL 14 Professional Plaza, 3790 Woodward Ave., Detroit, Mich. 48201.

Publication Committee: R. H. Greenspan, J. O. Reed, R. N. Cooley, P. A. Riemenschneider, J. F. Roach, Chairman, Albany, N. Y.

Finance and Budget Committee: R. L. Tondreau, W. B. Seaman, G. E. Sheline, J. M. Dennis, T. M. Fullenlove, Chairman, San Francisco, Calif.

Committee on Scientific Exhibits: R. E. Parks, R. G. Lester, W. N. Hanafee, Chairman, UCLA Medical Center, Los Angeles, Calif. 90024.

Advisory Committee on Education and Research: E. C. Klatte, A. R. Margulis, D. M. Witten, F. J. Bonte, C. M. Nice, Jr., Chairman, New Orleans, La.

Representatives on the American Board of Radiology: J. F. Roach, Albany, N. Y.; S. W. Nelson, Columbus, Ohio; and C. A. Stevenson, Spokane, Wash.

Director of Instruction Courses: H. O. Peterson, Minneapolis, Minn.; *Associate Director:* D. G. Mosser, Minneapolis, Minn.

Manager of the Annual Meeting: E. F. Lang, LL 14 Professional Plaza, 3790 Woodward Ave., Detroit, Mich. 48201.

Editor: T. Leucutia, 401 Professional Building, Detroit, Mich. 48201.

Representative on the Board of Chancellors of the American College of Radiology: S. F. Ochsner.

Seventieth Annual Meeting: Washington-Hilton Hotel, Washington, D. C., September 30–October 3, 1969.

AMERICAN RADIUM SOCIETY

President: Juan A. del Regato, Colorado Springs, Colo.; *President-Elect:* Fernando G. Bloedorn, Boston, Mass.; *1st Vice-President:* Clifford L. Ash, Toronto, Ont., Canada; *2nd Vice-President:* H. Peter Mueller, Boston, Mass.; *Secretary:* John V. Blady, The Parkway House, 2201 Benjamin Franklin Parkway, Philadelphia, Pa. 19130; *Treasurer:* James F. Nolan, 1407 South Hope St., Los Angeles, Calif. 90015.

Executive Committee: Justin J. Stein, Chairman, Los Angeles, Calif.; Juan A. del Regato; Fernando G. Bloedorn; Clifford L. Ash; H. Peter Mueller; John V. Blady; James F. Nolan; Milton Friedman; John L. Pool.

Scientific Program Committee: Juan A. del Regato, Chairman; Fernando G. Bloedorn, Vice-Chairman; Simon Kramer; Wm. E. Powers; Felix N. Rutledge; Jerome M. Vaeth.

Arrangements Committee: Luther W. Brady, Chairman, Philadelphia, Pa.; Gordon Verity, Chairman Designate; Larry McGowan; David Sklaroff; Antolin Raventos; James F. Nolan.

Publication Committee: Harry Hauser, Chairman, Cleveland, Ohio; Giulio J. d'Angio; William T. Moss.

Public Relations Committee: Antolin Raventos, Chairman; Robert Robbins; Harvey P. Groesbeck; Gordon Verity, *ex officio.*

Janeway Lecture Committee: Clifford L. Ash, Chairman, '69, Toronto, Ont., Canada; A. N. Arneson, '71; Milford D. Schulz, '73.

Representatives on the American Board of Radiology: Justin J. Stein, Los Angeles, Calif.; Ralph M. Scott, Louisville, Ky.; E. Richard King, Richmond, Va.

Liaison Representatives on the National Council on Radiation Protection and Measurements: Herbert M. Parker, Richland, Wash.; Marvin M. D. Williams, Rochester, Minn.

Representative on the Board of Chancellors of the American College of Radiology: Charles G. Stetson.

Fifty-first Annual Meeting: Bellevue Stratford Hotel, Philadelphia, Pa., April 28–30, 1969.

EDITORIALS

WHO SHOULD DO ECHOGRAPHY?

MANY different applications of ultrasound in the diagnosis of disease and investigation of anatomic structures have been developed in the last 15 years. Ultrasound is being used by physical therapists as a method of treatment. In laboratories it is used for cleaning instruments or breaking up red blood cells, in industry for testing purposes and to provide for compaction of various materials. On the diagnostic side, the "A" scan has been used for some years quite routinely as a method for determining midline structure position in the brain and in an attempt to differentiate solid from cystic masses in the field of obstetrics, as well as to determine the size of the fetal head. It may be possible to detect calcifications in arteries, such as in the internal carotid artery. The use of the Doppler effect with ultrasound permits the detection and measurement of flow of blood in various parts of the body—such as in the umbilical vessels of the fetus, in carotid arteries and other arteries of the body. The movements of the mitral valve and other portions of the heart can be outlined by using a time display of the "A" scan.

In recent years, there has been progressive development of "B" scan methods resulting in pictorial representation of various body structures.

Some of this work is being done by radiologists, a great deal of it is being done by specialists in other fields—cardiologists, obstetricians, renologists, and many investigators.

The question arises: In which area of medicine will these new modalities—such as ultrasound, thermography, and other new processes—fit best? A similar question has existed in the field of Nuclear Medicine.

The radiant energy used in echography is neither ionizing nor electromagnetic. Yet, the cross sectional representations of internal structures—at the present obtainable by the "B" scan method and, very likely, in the future, by holographic or other three dimensional displays—are in many ways related to the principles and methods employed in radiologic diagnosis.

The numerical or purely physiologic studies are often essentially laboratory tests, or, at times, minor extensions of physical diagnosis, and as such are of little or no interest to the radiologist except for special circumstances of either administrative nature or research application.

Thus, examinations such as the Doppler effect ultrasonic diagnosis of fetal life or death, analysis of cardiac flow patterns, and localization of intrarenal calculi at surgery will end up in the hands of the appropriate specialty fields. In the medical applications of radioactivity, blood volume determinations, Schilling and other such laboratory tests may well be of more interest to the clinical pathologist, the hematologist or physiologist than to the radiologist.

Our recent experience with ultrasound (see pages 438–445) suggests that the *pictorial* aspects of these procedures most suitably would fall in the province of the diagnostic radiologist. His general knowledge of anatomy, his experience and mental training in the analysis and three dimensional correlation of anatomic structures and pathologic changes are a real advantage in the interpretation of cross-sectional echographic displays, surface temperature patterns, specifically distributed radioactivity in internal organs and other pictorial

representations of the patient and his disease.

We would therefore suggest that the diagnostic radiologist be trained in, become familiar with and increase the application of pictorially represented diagnostic procedures, including those well established—such as roentgenology and isotope scanning—as well as newer methods. At the present time, echography, thermography and acoustic holography are in various stages of development. Due to their noninjurious nature, wide future application is expected. Subspecialization will very likely be necessary for full application of these new proliferating diagnostic modalities.

The field of the new pictorial diagnostic methods, particularly echography, is wide open. The diagnostic radiologist is the most suitable man to perform it. He ought to enter into it vigorously and contribute to its development.

Atis K. Freimanis, M.D.

Department of Radiology
Ohio State University Hospitals
410 West 10th Avenue
Columbus, Ohio 43210



W. WALTER WASSON, M.D.
1884–1968

ONE of the pioneers of radiology was lost to us on April 14, 1968 when Dr. W. Walter Wasson of Denver, Colorado, died. Dr. Wasson developed his interest in radiological work while he was in general practice in Boulder, Colorado, in about 1910. At that time he was using an electrostatic coil machine, unstable gas x-ray tubes, glass plates, and large flat trays for processing the plates.

In 1916 Dr. Wasson moved to Denver, Colorado, and limited his practice to radiology. There he established the Departments of Radiology at St. Anthony's Hospital

and at the Children's Hospital, and over the years served as consultant to most of the hospitals in Denver.

Dr. Wasson was born on a farm in Chrisman, Illinois, on August 17, 1884. He received his primary education in the local schools before entering Northwestern Academy in Evanston, Illinois, from which he graduated in 1904. At that time he decided to become a doctor, and did his premedical work at the University of Illinois, but obtained his Bachelor of Arts degree and his M.D. degree from the University of Colorado in 1910.

Dr. Wasson was a remarkable radiologist because he was a physician first, and enjoyed his contacts with patients. His devotion to them and to his profession was one of his outstanding qualities. No one ever questioned his integrity, and he was always a strong voice in insisting that the welfare of the patient came first. He possessed the quality of leadership, and exercised it effectively in the direction of the many radiological organizations to which he devoted his attention.

He maintained throughout his career a deep interest in research and in advancing radiologic techniques and in perfecting radiological procedures. He was a Founder of the Selmene Winter Foundation in 1922, of the Child Research Council in 1928, and a member of the Committee on Growth and Development of the 1929 White House Conference on Child Health and Protection.

With his partner, Dr. John S. Bouslog, he pioneered in developing the short exposure technique, and together they achieved the first 1/20 second chest roentgenogram. This enabled him to develop a most valuable collection of chest and bone roentgenograms on growing children.

Dr. Wasson was a person who could stimulate his colleagues and young men to develop an interest in the problems he was studying. He encouraged them and assisted them in their work, and was unselfish in supporting their developments.

In later years Dr. Wasson became interested in the radiation treatment of cancer, particularly in the treatment of cancer of the cervix in which he became an expert. His conscientious attention to details and to the general care of the patients brought him an unusual measure of success in this field.

In recognition of his contributions to radiology Dr. Wasson was awarded the Gold Medal of the Radiological Society of North America in 1926 for his developments in the diagnosis of pulmonary diseases in children. In 1958 he received the Gold Medal of the American College of Radiology for distinguished service to the specialty, and in 1960 was given the Norlin Recognition Medal of the Associated Alumni of the University of Colorado for outstanding distinction in his profession. In 1956 he organized with his contemporaries "The Gas Tube Gang," which later became the Council for Radiologic Heritage.

Dr. Wasson was always active in medical organizations, believing that they advanced the science of radiology and attracted bright young men to the specialty. He was one of the 25 Founders of the American College of Radiology and was a Chancellor from 1923–1931 and again from 1943–1947. He served as Chairman of the Section on Radiology of the American Medical Association from 1947 to 1948 and was a member of many organizations, both local and national, including the American Roentgen Ray Society and the American Medical Editors Association, and was an honorary member of Sigma Xi.

Dr. Wasson participated in the founding of the Radiological Society of North America, becoming President in 1941–1942. He was also active in the development of the Rocky Mountain Radiological Society, and was President in 1953. One wonders when reading his biography in Who's Who how he found time to participate in all of the organizations to which he belonged.

Dr. Wasson wrote many papers and gave many of them before local and national organizations. He enjoyed preparing these, and did it in an exact and detailed manner

and with a brevity that made them refreshing.

Dr. Wasson enjoyed the out-of-doors. He loved hunting, fishing, skating and horseback riding. Many of his colleagues were privileged to know his favorite horse, Ole Moss Charley. He played professional baseball prior to graduation from medical school and was a pitcher on both the University of Illinois and the University of Colorado baseball teams.

The mountains fascinated him. He and his wife, Katherine, built a beautiful home in the foothills of the Rocky Mountains west of Denver where he entertained his friends and to which he retired in the latter years of his life, and where Mrs. Wasson has continued to live. She was his gracious hostess, and shared his interest in medical and social activities as well as in the field of sports.

He is survived by his wife; twins, Richard Van Cleave of Yakima, Washington, and Madolin Layne (Mrs. Richard) Des Jardins, 5 grandchildren and 11 great-grandchildren, all of whom were a delight to him.

Radiology has lost but will not forget W. Walter Wasson, M.D., physician, radiologist, scientist, scholar, organizer and sportsman.

Wendell G. Scott, M.D.

100 N. Euclid Avenue
St. Louis, Missouri 63108

NEWS ITEMS

NEW OFFICERS OF THE RADIOLOGICAL SOCIETY OF NORTH AMERICA

At the Fifty-fourth Annual Meeting of the Radiological Society of North America held December 1–6, 1968, at the Palmer House in Chicago, Illinois, the following officers were elected: *President*—John H. Gilmore, M.D., Oak Park, Illinois; *President-Elect*—John R. Hodgson, M.D., Rochester, Minnesota; *First Vice-President*—John W. Beeler, M.D., Indianapolis, Indiana; *Second Vice-President*—John H. Walker, M.D., Seattle, Washington; *Third Vice-President*—Karl C. Corley, M.D., Washington, D.C.; *Secretary*—Maurice D. Frazer, M.D., Lincoln, Nebraska; *Treasurer*—R. Brian Holmes, M.D., Toronto, Ontario, Canada; and *Historian*—Howard P. Doub, M.D., Detroit, Michigan.

The *Chairman of the Board of Directors* is Reynold F. Brown, M.D., San Francisco, California.

The Gold Medal of the Society was awarded to Laurence L. Robbins, M.D., Boston, Massachusetts.

The Fifty-fifth Annual Meeting of the Society will be held at the Palmer House in Chicago, Illinois, November 30–December 5, 1969.

INTERNATIONAL SOCIETY OF LYMPHOLOGY

A course in "Lymphographical Diagnosis" will be held by the International Society of Lymphology in Davos, Switzerland, March 24–29, 1969.

For further information please contact Dr. A. Rüttimann, the Secretary-General, P.O. Box 128, 8028 Zurich, Switzerland.

SYMPOSIUM ON CURRENT CONCEPTS IN BONE AND JOINT DISEASE

The Department of Radiology, in cooperation with the Departments of Orthopedics and Pathology of the University of Kentucky Medical Center, is presenting a Symposium on "Current Concepts in Bone and Joint Disease," April 29–May 2, 1969, just before the Kentucky Derby.

A distinguished Visiting Faculty and staff members of the College of Medicine will participate in this Symposium.

The subject matter will include the arthritides, trauma, and chondrodysplasias, among others. One day will be devoted to a Panel Discussion by Radiologists and Pathologists on the nuances of a variety of proven cases. New or controversial material will be emphasized.

The Visiting Faculty includes: Dr. Ernest Aegerter, Temple University School of Medicine, Philadelphia, Pennsylvania; Dr. John Caffey, University of Pittsburgh, Pittsburgh, Pennsylvania; Dr. Lawrence Davis, University of Louisville School of Medicine, Louisville, Kentucky; Dr. Richard D. Gerle, Crouse-Irving Memorial Hospital, Syracuse, New York; Dr. James Harkess, University of Louisville School of Medicine, Louisville, Kentucky; Dr. John F. Holt, University of Michigan, Ann Arbor, Michigan; Dr. John Howieson, Yale University School of Medicine, New Haven, Connecticut; Dr. William Martel, University of Michigan, Ann Arbor, Michigan; Dr. Philip Rubin, University of Rochester School of Medicine, Rochester, New York; Dr. Eugene Slusher, Radiologist, Lexington Clinic, Lexington, Kentucky; Dr. Joseph A. Spinzia, Captain, U.S. Army, Fort Knox, Kentucky; and Dr. Aaron Weinstein, University of Cincinnati College of Medicine, Cincinnati, Ohio.

For further information please write to Harold D. Rosenbaum, M.D., Professor and Chairman, Department of Radiology, Medical Center, University of Kentucky, Lexington, Kentucky 40506.

POSTGRADUATE COURSE ON NUCLEAR MEDICINE AND DISEASES OF THE THYROID

A Postgraduate Course on "Nuclear Medicine and Diseases of the Thyroid" will

be held at the University of Michigan School of Medicine, Ann Arbor, Michigan, May 15 and 16, 1969.

This course is a review and discussion of the progress in diagnostic, experimental, and therapeutic use of radionuclides in medicine.

The discussions are illustrated with examples of the use of radionuclides in clinical and experimental studies.

The course includes a thorough appraisal of the new developments in the diagnosis and therapy of thyroid disease. The program should be of interest to the family physician, internist, radiologist, pediatrician, surgeon, and pathologist.

The Director of the course is William H. Beierwaltes, M.D., Professor of Medicine and Director of Nuclear Medicine, University of Michigan.

Inquiries regarding the course should be directed to the Department of Postgraduate Medicine, University of Michigan Medical Center, Ann Arbor, Michigan 48104.

CARDIAC ROENTGENOLOGY

The Continuing Education in Medicine University Extension, and The School of Medicine, UCLA in cooperation with The American College of Cardiology present "Cardiac Roentgenology," May 23–25, 1969, at the Century Plaza Hotel, Los Angeles, California.

The program deals with the scope of roentgen examination of the heart, including techniques, normal roentgen anatomy, and the roentgen findings in heart disease of various types.

The clinical evaluation of the results of roentgen examination and the assistance which it can render, both in specific diagnosis and in the outline of management will be discussed. A review of specific roentgen findings with plain roentgenograms, catheterization data, and angiography will be presented.

The Course Chairman is Leo G. Rigler, M.D.

The Guest Speakers will include: Kurt Amplatz, M.D., Minneapolis, Minnesota; Larry P. Elliott, M.D., Gainesville, Florida; Melvin Judkins, M.D., Portland, Oregon; Oscar Magidson, M.D., Los Angeles, California; and H. J. C. Swan, M.D., Los Angeles, California.

For further information please contact University Extension, UCLA, 10851 Le Conte Avenue, Los Angeles, California 90024.

IN VITRO PROCEDURES WITH RADIOISOTOPES IN CLINICAL MEDICINE AND RESEARCH

This Symposium, organized by the International Atomic Energy Agency (IAEA), will be held in Vienna, September 8–12, 1969.

The Symposium will be concerned with all procedures with radioisotopes in clinical medicine and research in which the radioactive material is added to the sample *in vitro* but is not administered to the subject. The topics to be covered include saturation analysis, dilution analysis, derivative analysis, radioimmunoassay, studies of enzyme activity, immunologic studies and cytologic studies on isolated tissues.

The Symposium will deal both with the procedures themselves and with their applications, and will give emphasis to procedures which have direct applications in clinical medicine and research. Neutron activation analysis will be excluded from the program.

Further information and forms to accompany abstracts of papers intended for presentation at the Symposium may be obtained from national authorities for atomic energy matters. Abstracts must be submitted through these authorities so as to reach the International Atomic Energy Agency before May 1, 1969.

For further information please write to the Scientific Secretaries: Dr. E. H. Belcher and Dr. T. Nagai, Section of Nuclear Medicine, Kärntnerring 11–13, 1010 Vienna, Austria.

INTERNATIONAL MEETING: COMPUTERS IN RADIOLOGY

An International Meeting on Computers in Radiology, organized by The Royal Belgian Society of Radiology, under the auspices of the European Association of Radiology will be held September 18–20, 1969 at the Palais des Congrès, Brussels, Belgium.

The purpose of the meeting is: To make an appraisal of the current use of computers in the field of radiology and to discuss the prospects for the future; to study the application of computerization in the various branches of radiology (therapy, nuclear medicine, diagnostic, etc.) and to review its possibilities in the more general fields of medical records, bibliography etc. as related to radiology; and to study the part played by the radiologist in the use of computers in the hospital service.

The proceedings will be of interest to radiologists, hospital administrators (whether medical or not) and to anyone faced with the prospect of computerization within his hospital group and the possibilities of its application to the radiologic disciplines.

The Scientific Committee will be responsible for coordinating and selecting reports and papers for presentation.

It would greatly help the meeting organizers if anyone wishing to present a paper would send the title accompanied by an abstract (maximum 200 words) and if possible a French translation, indicating also the size of slides.

The official languages of the conference will be those of the European Association of Radiology—French, German and English—and simultaneous translation will be provided in all three.

A social program, of particular interest to the ladies, is in the course of preparation.

The registration form, including hotel reservation, will be available with a provisional program in February, 1969.

All correspondence should be addressed to: Colloque de Radiologie, 64, chaussée de Haecht, Bruxelles 3, Belgium.

SYMPOSIUM ON THE USE OF CYCLOTRONS IN MEDICINE

A Symposium on the "Use of Cyclotrons in Medicine" will be held at Hammersmith Hospital, London, England on September 20, 1969.

It is intended to cover work in all medical fields. Particular topics will include medical uses of cyclotron produced isotopes and radiotherapy with fast neutrons.

The Symposium date has been chosen to precede the International Conference on the use of cyclotrons in chemistry, metallurgy and biology which is being organized by Atomic Energy Research Establishment at Oxford, September 22 and 23, 1969.

Further information may be obtained from R. J. Post, M.R.C. Cyclotron Unit, Hammersmith Hospital, Ducane Road, London W. 12, England.

BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

Surgical and Allied Malpractice. By Bernard J. Ficarra, A.B., Sc.B, LL.B, M.D., Sc.D, Ph.D., LL.D., J.D., Diplomate of the American Board of Surgery; Fellow of the American College of Legal Medicine; Fellow of the International Academy of Law and Science; Member of the Society of Medical Jurisprudence; Research Associate, Post-Graduate School, Long Island University, Greenvale, Long Island, N. Y. With forewords by Felix Forte, Associate Justice of the Superior Court, Commonwealth of Massachusetts, and Anthony J. DiGiovanna, Justice of the Supreme Court of the State of New York, Second Judicial District. Cloth. Pp. 1,234. Price, $60.00. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill. 62703, 1968.

Recent decades have witnessed astounding progress in medicine, surgery, and allied specialties comparable to our other space age achievements. Paralelling this progress has been a massive increase in medicolegal implications and malpractice actions. As physicians we are increasingly exposed to articles in lay magazines and newspapers as well as medical periodicals and news media relative to the dangers and prevention of malpractice suits. Within recent years many texts have dealt with various aspects of the subject, but this text is undoubtedly one of the most detailed, comprehensive, important and interesting ever written.

It is doubtful that an author not eminently qualified in both medicine and law could produce such a masterful work as did Dr. Ficarra. Although only 16 pages are exclusively devoted to medicolegal aspects of radiology, the context is such that radiologists as well as all other specialists and generalists will benefit from it.

The book has been divided into 6 Sections, the initial one dealing with general medicolegal knowledge relating primarily to surgical malpractice.

Section II relates to general jural procedures such as licensure, expert witnesses, standards of medical practice, courtroom procedures, privileged communications, statutes of limitations, legal doctrines, and morality in medicine, to name a few.

Section III deals with sources of malpractice according to regional anatomy and certain specific specialties. Of the 13 chapters in this section, included among the various subjects are pitfalls in x-ray diagnosis of the back, vascular roentgenology and lymphangiography, gastrointestinal bleeding, management of T-tubes, pulmonary embolism, foreign bodies, and esophageal diagnosis.

In Section IV the chapters are concerned with anesthesia, transfusions, oral surgery, hospital culpability, nursing pathology, preventive medicine, and finally radiology.

Sections V and VI comprise about one-third of the text and deal with various legal as well as moral issues including fraud, libel, agency, euthanasia, addiction, breach of contract, sterilization, experimentation, insurance, fee splitting and many others.

The text is documented with case histories and precedent setting legal decisions. This, of course, promotes reader interest, no matter where the book is opened. It contains moral wisdom founded on logic, and surgical knowledge enriched by experience.

Dr Ficarra has in this work attempted to benefit his profession by preventing malpractice actions against doctors and by giving a rebirth into its proper perspective the unblemished image of the doctor.

This reference text is well worth the monetary investment and should be owned by every active physician.

Arch H. Hall, M.D.

Physical and Photographic Principles of Medical Radiography. By Herman E. Seemann, Former Research Associate, Kodak Research Laboratories. Cloth. Pp. 132, with some illustrations. Price, $9.50. John Wiley & Sons, Inc., Publishers, 605 Third Avenue, New York, N. Y. 10016, 1968.

This is a concise, clear discussion of fundamental concepts in medical radiography. The

book is easy to read and contains a minimum of theoretical detail.

Although it is elementary, it is reasonably accurate and is sufficient for the needs of the average physician training in radiology. It is recommended for the latter and those wishing to obtain a background of information in this area.

William Martel, M.D.

BOOKS RECEIVED

Cerebral Blood Flow and Cerebro-Spinal Fluid. Third International Symposium, Lund-Copenhagen, May 9–11, 1968. Edited by D. H. Ingvar, N. A. Lassen, B. K. Siesjö, and E. Skinhøj. Scandinavian Journal of Clinical & Laboratory Investigation, 1968, Volume 22, Supplement 102.

Ultrasoft X Rays: An Historical and Critical Review of the World Experience with Grenz Rays and Other X Rays of Long Wavelength. By Mark B. Hollander, M.D., Assistant Professor of Dermatology, University of Maryland School of Medicine; Instructor in Dermatology, Johns Hopkins University School of Medicine, Baltimore, Md. Cloth. Pp. 198, with some illustrations. Price, $10.50. The Williams & Wilkins Company, 428 E. Preston Street, Baltimore, Md. 21202, 1968.

The Journal of Bone and Joint Surgery. Quinquennial Index, 1963–1967, Volumes 45–49. American Editorial Office, 10 Shattock Street, Boston, Mass., 1968.

Routine Surveillance for Radionuclides in Air and Water. World Health Organization, Geneva. Paper. Pp. 64. Price, $2.75. Available through: The American Public Health Association, Inc., 1740 Broadway, New York, N. Y. 10019, 1968.

Introduction to Medical Decision Making. By Lee B. Lusted, M.D., Professor and Chairman, Department of Radiology, Stritch School of Medicine, Loyola University Medical Center, Hines, Ill. Cloth. Pp. 722. Price, $18.75. Charles C Thomas, Publisher, 301-327 East Lawrence Avenue, Springfield, Ill. 62703, 1968.

The Radiologic Clinics of North America. Symposium on Radiology of the Heart. Guest Editor, Larry P. Elliott, M.D. Cloth. Pp. 216, with many illustrations. December, 1968, Volume VI, Number 3. W. B. Saunders Company, West Washington Square, Philadelphia, Pa. 19105, 1968.

Proceedings of the First International Congress of Radiation Protection. In two volumes. Sponsored by the International Radiation Protection Association at Rome, Italy, September 5–10, 1966. Edited by W. S. Snyder (U.S.A.), H. H. Albee (U.S.A.), L. K. Burton (U.K.), R. Maushart (Germany), A. Benco (Italy), F. Duhamel (France), and B. M. Wheatly (U.K.). Cloth. Pp. 1624, with many figures. Price, $65.00. Pergamon Press Inc., 44–01 21st Street, Long Island City, N. Y. 11101, 1968.

Annual Review of Nuclear Science. Emilio Segrè, Editor. J. Robb Grover, and H. Pierre Noyes, Associate Editors. Volume 18. Cloth. Pp. 554, with some figures. Price $8.50, U.S.A., $9.00 Foreign. Annual Reviews, Inc., 4139 El Camino Way. Palo Alto, Calif., 1968.

The Curability of Cancer in Various Sites. Fourth statistical report of the Christie Hospital and Holt Radium Institute, Manchester. By Eric C. Easson, M.D., M.R.C.P. (Glasg.), F.F.R., Director of Radiotherapy, Christie Hospital and Holt Radium Institute; and the late Marion H. Russell, A.E.S., F.S.S., Head, Department of Statistical Research, Christie Hospital and Holt Radium Institute. Cloth. Pp. 150, with some figures. Price, 35s. Pitman Medical Publishing Company, Ltd., 46 Charlotte Street, London, W1, England, 1968.

Fundamental Problems in Scanning. Compiled and Edited by Alexander Gottschalk, M.D., Associate Professor of Radiology; Director, Argonne Cancer Research Hospital; Director, Section of Nuclear Medicine, Department of Radiology, University of Chicago, Chicago, Ill.; and Robert N. Beck, B.S., Associate Professor of Radiological Sciences, Department of Radiology and Argonne Cancer Research Hospital, University of Chicago, Chicago, Ill. Based on a Symposium sponsored by the Argonne Cancer Research Hospital (operated by the University of Chicago for the United States Atomic Energy Commission), The Northwestern University School of Medicine, and Abbott Laboratories. Cloth. Pp. 410, with some figures. Price, $26.75. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill. 62703, 1968.

Die gesunde und die kranke Wirbelsäule in Röntgenbild und Klinik. Begründet von Georg Schmorl. Cloth. Pp. 556, with 500 figures. Price, DM 110.-. Georg Thieme Verlag, Herdweg 63, Stuttgart 1, Germany, 1968.

L'Artériographie dans les Affections Chirurgicales du Foie, du Pancréas et de la Rate. By Jacques Hepp, Claude Hernandez, Jean Moreaux, and Henry Bismuth. Paper. Pp. 194, with 114 figures. Price, 80 F. Masson & Cie, Editeurs, 120, Boulevard Saint-Germain, Paris, 1968.

Molekulare Struktur und Strahlenwirkung. By H. Glubrecht, D. Ernst, H. Hinsch, M. Knälmann, W. Scheurmann, and W. Siebert. Paper. Pp. 228, with 111 figures. Price, DM 32.-. Georg Thieme Verlag, Herdweg 63, Stuttgart 1, Germany, 1968.

La Sottrazione d'Immagine in Angiografia Cerebrale Simultanea. By Giovanni Ruggiero, and Pietro Dettori, Bologna, Italy. Cloth. Pp. 322,

with many figures. Cappelli editore, Bologna, Italy, 1966.

MALIGNANT LYMPHOMAS AND THEIR MANAGEMENT. By Melville L. Jacobs. Recent Results in Cancer Research. Volume 16. Cloth. Pp. 48, with 7 figures. Price, $4.50. Springer-Verlag New York Inc., 175 Fifth Avenue, New York, N. Y. 10010, 1968.

ROENTGEN TECHNIQUES IN LABORATORY ANIMALS. Radiography of the dog and other experimental animals. Planned by the Committee for the Preparation of a Technical Guide for Roentgen Techniques in Laboratory Animals. Veterans Administration, Department of Medicine and Surgery, Research and Education in Medicine. Edited by Benjamin Felson, M.D. Cloth. Pp. 245, with many figures. Price, $17.50. Canadian Price, $18.90. W. B. Saunders Company, West Washington Square, Philadelphia, Pa. 19105, 1968.

SOCIETY PROCEEDINGS

MEETINGS OF RADIOLOGICAL SOCIETIES*

UNITED STATES OF AMERICA

AMERICAN ROENTGEN RAY SOCIETY
Secretary, Dr. Ted F. Leigh, Emory University Clinic, Atlanta, Ga. 30322. Annual Meeting: Washington-Hilton Hotel, Washington, D.C., September 30–October 3, 1969.

AMERICAN RADIUM SOCIETY
Secretary, Dr. John V. Blady, The Parkway House, 2201 Benjamin Franklin Parkway, Philadelphia, Pa. 19130. Annual meeting: Bellevue Stratford Hotel, Philadelphia, Pa., April, 28–30, 1969.

RADIOLOGICAL SOCIETY OF NORTH AMERICA
Secretary-Treasurer, Dr. Maurice Doyle Frazer, 1744 South Fifty-eighth St., Lincoln, Neb. Annual meeting: Palmer House, Chicago, Ill., November 30–December 5, 1969.

AMERICAN COLLEGE OF RADIOLOGY
Executive Director, William C. Stronach, 20 N. Wacker Drive, Chicago 6, Ill. Annual meeting: Regency Hyatt House, Atlanta, Ga., Feb. 18–22, 1969.

SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION
Secretary, Dr. Kenneth L. Krabbenhoft, Harper Hospital, Detroit, Mich. 48201. Annual meeting: New York, N. Y., July 13–17, 1969.

AMERICAN BOARD OF RADIOLOGY
Secretary, Dr. C. Allen Good. Correspondence should be directed to Kahler Center Building, Rochester, Minn. 55901.

The oral examinations will be held at the Pittsburgh Hilton Hotel, Pittsburgh, Pa., June 2–6, inclusive, 1969; and at the Statler Hilton Hotel, Dallas, Texas, Dec. 8–12, inclusive, 1969.

The written examination will be held in selected sites, Saturday, June 21, 1969.

The deadline for filing applications for any of the above three examinations was December 31, 1968.

AMERICAN ASSOCIATION OF PHYSICISTS IN MEDICINE
Secretary, Leonard Stanton, Hahnemann Medical College, 230 N. Broad St., Philadelphia, Pa. 19102.

AMERICAN SOCIETY OF THERAPEUTIC RADIOLOGISTS
Secretary, Dr. J. A. del Regato, Penrose Cancer Hospital, Colorado Springs, Colo. 80907.

AMERICAN SOCIETY FOR DIAGNOSTIC ULTRASOUND
Secretary, Dr. Charles C. Grossman, 552 N. Neville St., Pittsburgh, Pa. 15213.

AMERICAN SOCIETY OF NEURORADIOLOGY
Secretary-Treasurer, Dr. Alan E. Zimmer, Danbury, Conn. 06810.

TWELFTH INTERNATIONAL CONGRESS OF RADIOLOGY
President, Dr. Kempo Tsukamoto, 9-1, 4-chome, Angewa, Chiba, Japan. Meeting: Hotel New Otani, Tokyo, Japan, Oct. 6–11, 1969.

TENTH INTER-AMERICAN CONGRESS OF RADIOLOGY
Counselor for the United States, Dr. Juan A. del Regato, Penrose Cancer Hospital, 2215 North Cascade Ave., Colorado Springs, Colo. 80907.
President, Dr. Juan A. del Regato, Colorado Springs, Colo., USA.
Secretary, Dr. F. Bloedorn, Boston, Mass., USA.
Meeting: San Juan, Puerto Rico, 1971.

INTER-AMERICAN COLLEGE OF RADIOLOGY
President, Dr. Oscar Soto, H. Urteaga 480, Lima, Perú.

ALABAMA RADIOLOGICAL SOCIETY
Secretary, Dr. Walter Brower, Birmingham, Ala. Meets time and place of Alabama State Medical Association.

ALASKA RADIOLOGICAL SOCIETY
Secretary, Dr. Bruce C. Wright, Providence Hospital, Anchorage, Alaska. Meets third Wednesday each month.

ARIZONA RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Robert E. Steyskal, 550 W. Thomas Rd., Phoenix, Ariz. 85013. Two regular meetings a year. Annual meeting at time and place of State Medical Association and interim meeting six months later.

ARKANSAS CHAPTER OF AMERICAN COLLEGE OF RADIOLOGY
Secretary-Treasurer, Dr. Wilma C. Diner, Univ. of Arkansas Medical Center, Little Rock, Ark. 72201.

ARKANSAS RADIOLOGICAL SOCIETY
Secretary, Dr. Charles W. Anderson, 1108½ Poplar, Pine Bluff, Ark. Meets every three months and also at time and place of State Medical Association.

ASSOCIATION OF UNIVERSITY RADIOLOGISTS
Secretary-Treasurer, Dr. Alexander Gottschalk, University of Chicago Medical School, Chicago, Ill. 60637. Annual Meeting: University of California, San Francisco, May 7–10, 1969.

ATLANTA RADIOLOGICAL SOCIETY
Secretary, Dr. Donald R. Rooney, Burnt Hickory Road, Marietta, Ga. Meets monthly except during three summer months, on third Tuesday, at the Academy of Medicine, Atlanta, Ga., at 8:00 P.M.

BAVARIAN-AMERICAN RADIOLOGIC SOCIETY
Advisor, Colonel Paul E. Sieber. *Secretary*, Major Peter B. Riesz, USAH Bad Cannstatt, APO 09154, New York. N. Y. Meets quarterly.

BLOCKLEY RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. R. John Gould, 41 Lombardy Rd., Drexel Hill, Pa. 19026.

BLUEGRASS RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Joe Bernard, Central Baptist Hosp., Lexington, Kentucky 40503. Meets quarterly.

BROOKLYN RADIOLOGICAL SOCIETY
Secretary, Dr. Coleman H. Rosenberg, 81–10 Chevy Chase St., Jamaica, N.Y. 11432. Meets first Thursday of each month, October through June.

BUFFALO RADIOLOGICAL SOCIETY
Secretary, Dr. Courtland Van Deusen, 817 Main St., Niagara Falls N. Y. 14301. Meets second Monday evening each month, October to May inclusive., at University Club.

CALIFORNIA RADIOLOGICAL SOCIETY
Secretary-Treasurer: Dr. Leroy K. Mills, 3157 Oakcliff Circle, Carmichel, Calif. 95608. Meets annually during meeting of California Medical Association.

CATAWBA VALLEY RADIOLOGICAL SOCIETY
Secretary, Dr. Emmett R. White, P. O. Box 303, Rutherford College, N. C. 28671. Meets every Friday, Dept. of Radiology, Valdese General Hosp., Valdese, N. C., at 12:00 NOON.

CENTRAL NEW YORK RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. George, Mitchell, Radiology Department, Syracuse Memorial Hospital, Syracuse, N. Y. 13210. Meets first Monday each month, October through May.

CENTRAL OHIO RADIOLOGICAL SOCIETY
Secretary, Dr. Ollie E. Southard, 2787 Tudor Rd., Columbus, O. 43209. Meets second Thursday in October, November, January, and March 15 and May 19 at Fort Hayes Hotel, Columbus, Ohio.

* Secretaries of societies are requested to send timely information promptly to the Editor.

Chicago Roentgen Society
Secretary-Treasurer, Dr. Howard C. Burkhead, 2650 Ridge Ave., Evanston, Ill. 60202. Meets third Wednesday of each month, October to April, except December, at the University Club of Chicago.

Cleveland Radiological Society
Secretary-Treasurer, Dr. James Farmer, 18869 Canyon Rd. Fairview Park, Ohio 44126. Meetings at 7:00 P.M. on fourth Monday of October, November, January, February, March and April.

Colorado Radiological Society
Secretary, Dr. Charles E. Seibert, Department of Radiology, Swedish Hospital, 501 E. Hampton, Englewood, Colo. 80110. Meets third Friday of each month at Denver Athletic Club from September through May.

Connecticut Valley Radiologic Society
Secretary, Dr. William W. Walthall, Jr., 130 Maple St., Springfield, Mass. Meets in April and October.

Dallas-Fort Worth Radiological Society
Secretary-Treasurer, Dr. R. W. Perrin, P.O. Box 5999, Dallas, Texas 75222. Meets the 3rd Monday of every month at 6:30 P.M., at the Cibola Inn, Arlington, Texas.

Detroit Roentgen Ray Society
Secretary, Dr. David P. Corbett, Harper Hospital, Detroit, Mich. 48201. Meets monthly, first Thursday, October through May, at David Whitney House, 1010 Antietam, at 6:30 P.M.

East Bay Radiological Society
Secretary, Dr. Allen B. Freitag, 411 30th Str., Oakland, Calif. 94609. Meets first Thursday each month, Oct. through May, at University Club, Oakland, Calif.

East Tennessee Radiological Society
Secretary-Treasurer, Dr. T. F. Haase, Jr., 205 Medical Arts Building, Knoxville, Tenn. Meets in January and September.

Florida Radiological Society
Secretary, Dr. Robert H. Nickau, Good Samaritan Hospital, West Palm Beach, Fla. 33402. Meets twice annually, in the spring with the annual State Society Meeting and in the fall.

Florida West Coast Radiological Society
Secretary-Treasurer, Dr. Allen L. Sheer, University Community Hospital, 13505 N. 31st St., Tampa, Fla. 33612. Meets in January, March, May, July, September and November.

Georgia Radiological Society
Chapter of the American College of Radiology
Secretary, Dr. Walker Harris, The Medical Center, Columbus, Georgia 31902. Meets in spring and fall at Annual State Society Meeting.

Greater Cincinnati Radiological Society
Secretary-Treasurer, Dr. Owen L. Brown, 2421 Auburn Ave., Cincinnati, Ohio 45219.

Greater Louisville Radiological Society
Secretary-Treasurer, Dr. L. D. LeNeave, 315 E. Broadway, Louisville, Ky. 40202. Meets monthly.

Greater Miami Radiological Society
Secretary-Treasurer, Dr. Sylvan H. Sarasohn, North Miami General Hospital, 1701 Northeast 127th St., North Miami, Fla. 33161. Meets monthly, third Wednesday at 8:00 P.M. at Jackson Memorial Hospital, Miami, Fla.

Greater St. Louis Society of Radiologists
Secretary-Treasurer, Dr. Roland P. Ernst, 3720 Washington Ave., St. Louis, Mo. 63108.

Hawaii Radiological Society
Secretary-Treasurer, Dr. Thomas C. Brown, 1697 Ala Moana Blvd., Honolulu, Hawaii 96815. Meets third Monday of each month at 7:30 P.M.

Health Physics Society
Secretary, R. J. Augustine, National Center for Radiologic Health, 1901 Chapman Ave., Rockville Md. 20852.

Houston Radiological Society
Secretary, Dr. Thomas S. Harle, 1200 Moursond Drive Houston, Tex. 77025. Meets fourth Monday of each month, except June, July, August and December, at the Doctors' Club, 8:00 P.M., Houston, Tex.

Idaho State Radiological Society
Secretary, Dr. George H. Harris, Bannock Memorial Hospital, Pocatello, Idaho. Meets in the spring and fall.

Illinois Radiological Society, Inc.
Secretary, Dr. C. R. Markivee, 674 North Seminary St., Galesburg, Ill. 61401. Meets in the spring and fall.

Indiana Roentgen Society, Inc.
Secretary, Dr. Edwin F. Koch, Jr., 915 University Ave., Muncie, Ind. 47303. Meets first Sunday in May and during fall meeting of Indiana State Medical Association.

Iowa Radiological Society
Secretary-Treasurer, Dr. J. H. Lohnes, 1948 First Ave., N.E., Cedar Rapids, Iowa 52402. Luncheon and business meeting during annual session of Iowa State Medical Society. The scientific section is held in the autumn.

Kansas Radiological Society
Secretary-Treasurer, Dr. Robert C. Lawson, 310 Medical Arts Bldg., 10th and Horne, Topeka, Kan. Meets in spring with State Medical Society and in winter on call.

Kentucky Chapter, American College of Radiology
Secretary-Treasurer, Dr. Ralph C. Quillin, 1221 S. Broadway, Lexington, Ky. 40504. Meets in April and September.

Kings County Radiological Society
Secretary, Dr. Sidney Hendler, 1880 Ocean Ave., Brooklyn 30, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

Knoxville Radiological Society
Secretary, Dr. Clifford L. Walton, Blount Professional Bldg., Knoxville 20, Tenn. Meetings are held the third Monday of every other month at the University of Tennessee Memorial Research Center and Hospital.

Long Island Radiological Society
Secretary, Dr. Robert J. Hochstim, 1200 Stewart Ave., Garden City, N. Y. 11533. Meets monthly.

Los Angeles Radiological Society
Secretary, Dr. John L. Gwinn, Childrens Hospital of Los Angeles, 4650 Sunset Blvd., Los Angeles, Calif. 90027. Meets second Wednesday of month in September, November, January, April and June at Los Angeles County Medical Association Building, Los Angeles, Calif.

Louisiana-Texas Gulf Coast Radiological Society
Secretary-Treasurer, Dr. Edward A. Sheldon, 109 Doctors Bldg., Beaumont, Texas 77701.

Maine Radiological Society
Secretary-Treasurer, Dr. Robert A. Bearor, Maine Medical Center, Portland, Maine 04102. Meets in June, September, December and April.

Maryland Radiological Society
Secretary, Dr. Henry Startzman, Medical Arts Building, Baltimore, Md.

Massachusetts Radiological Society
Secretary, Dr. Jerome H. Shapiro, Department of Radiology, Boston City Hospital, 818 Harrison Ave., Boston, Mass. 02118.

Memphis Roentgen Society
Secretary-Treasurer, Dr. Webster Riggs, Jr., The University of Tennessee College of Medicine, Department of Radiology, Walter F. Chandler Bldg., 865 Jefferson Ave., Memphis, Tenn. 38103. Meets first Monday of each month at John Gaston Hospital.

Miami Valley Radiological Society
Secretary, Dr. Darwood B. Hance, Reid Memorial Hospital, Richmond, Indiana. Meets third Thursday of fall, winter and spring months at 7:30 P.M. at Miami Valley Hospital, Dayton, Ohio.

Mid-Hudson Radiological Society
Secretary-Treasurer, Dr. Herbert S. Berlin, Hopewell Junction, N. Y. Meets 7:00 P.M., first Wednesday of each month, September to May.

Milwaukee Roentgen Ray Society
Secretary-Treasurer, Dr. James E. Bell, 8700 W. Wisconsin Ave., Milwaukee, Wis. 53213. Meets monthly on fourth Monday, October through May, at University Club.

Minnesota Radiological Society
Secretary-Treasurer, Dr. Warren L. Kump, 4243 Glenwood Ave., Minneapolis, Minn. 55422. Meets twice annually, fall and winter.

Mississippi Radiological Society
Secretary-Treasurer, Dr. Dan T. Keel, Jr., 504 Chippewa St., Brookhaven, Miss. Meets third Thursday of each month at the Heidelberg Hotel, Jackson, at 6:00 P.M.

Missouri Radiological Society
Secretary-Treasurer, Dr. Arthur A. Porporis, 100 N. Euclid Ave., St. Louis, Mo. 63108.

Montana Radiological Society
Secretary, Dr. Clark Grimm, Great Falls, Montana. Meets at least once a year.

Nebraska State Radiological Society
Secretary-Treasurer, Dr. Otto A. Troester, 924 Sharp Building, Lincoln, Nebraska 60508. Meets third Wednesday of each month at 6 P.M. in Omaha or Lincol c

Nevada Radiological Society
Secretary, Dr. William G. Arbonies, Department of Radiology, St. Mary's Hospital, Reno, Nev.

New England Roentgen Ray Society
Secretary, Dr. Morris Simon, 330 Brookline Ave., Boston, Mass. 02115. Meets third Friday of each month, October through May, at The Longwood Towers, 20 Chapel Street, Brookline, Mass., at 4:30 P.M. The Annual Meeting will be held May 24 and 25, 1969, at the Hotel Belmont, West Harwich by-the-sea, Cape Cod, Mass. The guest speaker, Dr. Lucy Frank Squire, will present the Twenty-fifth George W. Holmes Lecture.

New Hampshire Roentgen Ray Society
Secretary, Dr. Paul Y. Hasserjian, 1470 Elm St., Manchester, N. H. Meets four to six times yearly.

New Mexico Association of Radiologists
Secretary-Treasurer, Dr. Justin J. Wolfson, Department of Radiology, Bernalillo County-Indian Hospital, Albuquerque, New Mexico.

New Mexico Society of Radiologists
Secretary, Dr. Phil Fox, Albuquerque, New Mexico. Four meetings annually, three held in Albuquerque, N. M., and one held at time and place of New Mexico State Medical Society annual meeting.

New York Roentgen Society
Secretary-Treasurer, Dr. Samuel H. Madell, 1 E. 82nd St New York, N. Y. 10024. Meets monthly on third Monday at the New York Academy of Medicine at 4:30 P.M.

New York State Chapter of the American College of Radiology, Inc.
Secretary-Treasurer, Dr. John W. Colgan, 273 Hollywood Ave., Rochester, N. Y., 14618.

North Carolina Chapter of ACR.
Secretary-Treasurer, Dr. Ira Bell, Hickory, N. C.

North Carolina Radiological Society
Secretary, Dr. E. H. Schultz, North Carolina Memorial Hospital, Chapel Hill, N. C. Meets in the spring and fall each year.

North Dakota Radiological Society
Secretary, Dr. A. Ohrt, 408 Medical Arts Bldg., Fargo, N. D. 58102. Meets at time of State Medical Association meeting. Other meetings arranged on call of the President.

North Florida Radiological Society
Secretary, Dr. Charles H. Newell, 800 Miami Road, Jacksonville 7, Fla. Meets quarterly in March, June, September and December.

Northeastern New York Radiological Society
Secretary, Dr. Herbert F. Reilly, Jr., 12 Sandalwood Rd., Scotia, New York 12302. Meets in Albany area on third Wednesday of October, November, March, April, and May.

Northern California Radiological Society
Secretary-Treasurer, Ivan D. Siddons, 3701 J. St., Suite 106, Sacramento, Calif. 95816. Meets fourth Monday of Sept., Nov., Jan., March and May at the Sutter Club in Sacramento.

Northwestern Ohio Radiological Society
Secretary, Dr. Vito J. Zupa, Mercy Hospital, Department of Radiology, Toledo, Ohio.

Ohio State Radiological Society
Secretary, Dr. Robert D. Berkebile, Elyria Memorial Hospital, Elyria, Ohio 44035.

Oklahoma State Radiological Society
Secretary, Dr. Donald F. Mauritson, 100 Utica Square Med. Center, Tulsa, Okla. 74114. Meets in January, May and October.

Orange County Radiological Society
Secretary, Dr. George W. Logan, 301 Newport Blvd., Newport Beach, Calif. Meets fourth Tuesday of every month at Orange County Medical Association Building.

Oregon Radiological Society
Secretary-Treasurer, Dr. Clinton B. Sayler, 214 Medical Dental Bldg., Portland, Oregon 97205. Meets on second Wednesday of month, October through April, at the University Club, Portland, Ore.

Orleans Parish Radiological Society
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans, La. 70113. Meets second Tuesday of each month.

Pacific Northwest Radiological Society
Secretary-Treasurer, Dr. Marvin Wallace, 555 108th Ave. N. E., Bellevue, Washington 98004.

Pennsylvania Radiological Society
Secretary, Dr. Theodore A. Tristan, Harrisburg, Polyclinic Hosp., Harrisburg, Pa. 17105.

Philadelphia Roentgen Ray Society
Secretary, Dr. C. Jules Rominger, Misericordia Hospital, 54th St. and Cedar Ave., Philadelphia, Pa. 19143. Meets first Thursday of each month at 5 P.M., from October to May in Thompson Hall, College of Physicians.

Pittsburgh Roentgen Society
Secretary, Dr. Edward R. Seitz, 601 Jenkins Bldg., Pittsburgh, Pa. 15222. Meets second Wednesday of month, October through June, at Park Schenley Restaurant.

Radiation Research Society
Secretary-Treasurer, Dr. Gail D. Adams, Dept. of Radiology, Univ. of Oklahoma Medical Center, Oklahoma City, Oklahoma 73104. Annual Meeting: Netherland Hilton Hotel, Cincinnati, Ohio, May 18–22, 1969.

Radiological Society of Connecticut, Inc.
Secretary-Treasurer. Dr. Henry J. Fox, 10 Washington Ave., Bridgeport, Conn. Meetings are held quarterly.

Radiological Society of Greater Cincinnati
Secretary-Treasurer, Dr. Donald E. Gunderson, 3553 Bayard Dr., Cincinnati, Ohio 45208. Meets first Monday of each month at Cincinnati Academy of Medicine.

Radiological Society of Greater Kansas City
Secretary, Dr. J. Stewart Whitmore, 1010 Rialto Bldg., Kansas City, Mo. Meets last Friday of each month.

Radiological Society of Kansas City
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

Radiological Society of Louisiana
Secretary, Dr. Lester W. Eavenson, 2700 Napoleon Ave., New Orleans 15, La. Meets semiannually, during Louisiana State Medical Society meeting and 6 months later.

Radiological Society of New Jersey
Secretary, Dr. John W. Marquis, 12 Hawthorne Ave., East Orange, N. J. 07018. Meets in Atlantic City at time of State Medical Society meeting and in October or November in Newark, N. J.

Radiological Society of Rhode Island
Secretary-Treasurer, Dr. John M. Vesey, 1196 Elmwood Ave., Cranston, R. I.

RADIOLOGICAL SOCIETY OF SOUTH DAKOTA
Secretary-Treasurer, Dr. Donald J. Peik, 303 S. Minnesota Ave., Sioux Falls, S. D.

RADIOLOGICAL SOCIETY OF SOUTHERN CALIFORNIA
Secretary-Treasurer, Dr. Robert G. Williams, The Santa Barbara Medical Clinic, P.O. Box 1200, Santa Barbara, Calif. 93102. Meets three times a year, usually October, February and May.

RADIOLOGICAL SOCIETY OF THE STATE OF NEW YORK
Secretary-Treasurer, Dr. John W. Colgan, 273 Hollywood Ave., Rochester, N. Y. 14618.

REDWOOD EMPIRE RADIOLOGICAL SOCIETY
Secretary, Dr. Lee F. Titus, 164 W. Napa St., Sonoma, Calif. Meets second Monday every other month.

RICHMOND COUNTY RADIOLOGICAL SOCIETY
Secretary, Dr. W. F. Hamilton, Jr., University Hospital, Augusta, Ga. Meets first Thursday of each month at various hospitals.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.
Secretary, Dr. Kenneth E. Robinson, Rochester General Hospital, 1425 Portland Ave., Rochester, N. Y. 14621. Quarterly meetings on the call of the President, at the Rochester Academy of Medicine.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Robert W. Lackey, 4200 E. Ninth Ave., Denver, Colo. 80220. Annual meeting: Brown Palace Hotel, Denver, Colo., Aug. 21–23, 1969.

SAN ANTONIO-MILITARY RADIOLOGICAL SOCIETY
Secretary, Dr. Hugho F. Elmendorf, Jr., 730 Medical Arts Bldg., San Antonio 5, Tex. Meets third Wednesday of each month in Fort Sam Houston Officer's Club at 6:30 P.M.

SAN DIEGO RADIOLOGICAL SOCIETY
President-Secretary, Charles R. Henkelmann, 3909 Palm Drive, Bonita, Calif. 92002. Meets first Wednesday of each month at the Town & Country Motel.

SAN FRANCISCO RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Walter W. Herbert, Saint Francis Memorial Hospital, 900 Hyde St., San Francisco, Calif. 94109. Meets quarterly at the San Francisco Medical Society, 250 Masonic Ave., San Francisco, Calif. 94118.

SANTA CLARA COUNTY RADIOLOGICAL SOCIETY
Secretary, Dr. D. Brendan O'Donnell, 696 E. Santa Clara St., San Jose, Calif. 95112. Meets monthly at the Santa Clara County Medical Association Bldg., 700 Empey Way, San Jose, Calif.

SECTION ON RADIOLOGY, CALIFORNIA MEDICAL ASSOCIATION
Secretary, Dr. William H. Graham, 630 East Santa Clara St., San Jose, Calif.

SECTION ON RADIOLOGY, MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA
Secretary-Treasurer, Dr. Louis Wener, Cafritz Memorial Hosp., 1310 Southern Ave., S.E., Washington, D. C. 20032. Meets at Medical Society Library, third Wednesday of January, March, May and October at 8:00 P.M.

SECTION ON RADIOLOGY, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr. Phillip W. Voltz, Jr., 120 Medical Professional Bldg., San Antonio, Texas 78212. Annual meeting: To be announced.

SECTION ON RADIOLOGY, TEXAS MEDICAL ASSOCIATION
Secretary, Dr. George F. Crawford, St. Elizabeth Hospital, Beaumont, Tex. Meets annually with the Texas Medical Association.

SHREVEPORT RADIOLOGICAL CLUB
Secretary, Dr. W. R. Harwell, 608 Travis St., Shreveport, La. Meets monthly on third Wednesday at 7:30 P.M., September to May inclusive.

SOCIETY FOR PEDIATRIC RADIOLOGY
Secretary, Dr. John L. Gwinn, Children's Hospital, 4614 Sunset Blvd., Los Angeles 27, Calif. Annual meeting: Washington-Hilton Hotel, Washington, D.C., September 29, 1969.

SOCIETY OF NUCLEAR MEDICINE
Secretary, Mr. C. Craig Harris, Oak Ridge National Laboratories, Oak Ridge, Tenn. *Administrator*, Mr. Samuel N. Turiel, 430 N. Michigan Ave., Chicago 11, Ill. Annual meeting Jung Hotel, New Orleans La., June 22–28, 1969.

SOUTH BAY RADIOLOGICAL SOCIETY
Secretary, Dr. Emerson C. Curtis, University Dr., Menlo Park, Calif. 94025. Meets second Wednesday of each month.

SOUTH CAROLINA RADIOLOGICAL SOCIETY
Secretary, Dr. George W. Brunson, 1406 Gregg St., Columbia, S. C. Annual meeting (primarily business) in conjunction with the South Carolina Medical Association meeting in May. Annual fall scientific meeting at time and place designated by the president.

SOUTH DAKOTA RADIOLOGICAL SOCIETY
Secretary, Dr. Donald J. Peik, 1417 S. Minnesota Ave., Sioux Falls, S. Dak. Meets in spring with State Medical Society and in fall.

SOUTHERN CALIFORNIA RADIATION THERAPY SOCIETY
Secretary-Treasurer, Dr. Aaron G. Fingerhut, 1000 W. Carson St., Torrance, Calif. 90502. Meets quarterly.

SOUTHERN RADIOLOGICAL CONFERENCE
Secretary-Treasurer, Dr. Marshall Eskridge, Mobile Infirmary, P.O. Box 4097, Mobile, Ala. 36604. Annual meeting: Grand Hotel, Pointe Clear, Ala. 36564, Jan. 31–Feb. 2, 1969.

SOUTHWESTERN RADIOLOGICAL SOCIETY
Secretary, John M. McGuire, 904 Chelsea, El Paso, Tex. Meets last Monday of each month at 6:30 P.M. in the Paso del Norte Hotel.

TENNESSEE RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Marion E. Spurgeon, Memorial Hosp., Clarksville, Tenn. 37040. Meets annually at the time and place of the Tennessee State Medical Association meeting.

TEXAS RADIOLOGICAL SOCIETY
Secretary, Dr. Herman C. Sehested, 815 Medical Arts Bldg., Fort Worth 2, Tex. Annual meeting to be announced.

TRI-STATE RADIOLOGICAL SOCIETY
Secretary, Dr. John H. Marchand, Jr., Methodist Hospital, Henderson, Ky. Meets third Wednesday of Oct., Jan., March and May, 8:00 P.M., Elks Club in Evansville, Ind.

UNIVERSITY OF MICHIGAN DEPARTMENT OF ROENTGENOLOGY STAFF MEETING
Meets each Monday evening from September to June, at 7:00 P.M. at University Hospital, Ann Arbor Mich.

UPPER PENINSULA RADIOLOGICAL SOCIETY
Secretary, Dr. A. Gonty, Menominee, Mich. Meets quarterly.

UTAH STATE RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Leon M. Neal, St. Benedict's Hospital, 3000 Polk Ave., Ogden, Utah 84403. Meets fourth Wednesday in January, March, May, September and November at Holy Cross Hospital.

VERMONT RADIOLOGICAL SOCIETY
Secretary, Dr. John R. Williams, 160 Allen St., Rutland, Vt.

VIRGINIA RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. K. Kenneth Wallace Jr., Norfolk, Va.

WASHINGTON STATE RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Paul S. Paulson, 1001 Broadway, Seattle, Washington 98122. Meets quarterly.

WEST VIRGINIA RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. George G. Green, Department of Radiology, W. Va. Univ. Medical Center, Morgantown, W. Va. 26506. Meets concurrently with Annual Meeting of West Virginia State Medical Society; other meetings arranged by program committee.

WESTCHESTER COUNTY RADIOLOGICAL SOCIETY
Secretary, Dr. Arnold Gerson, Medical Arts Bldg., Mt.

Vernon, N. Y. Meets on third Tuesday of January and October and on two other dates.

Wisconsin Radiological Society
Secretary-Treasurer Dr. Robert E. Douglas, 117 N. Commerical St., Neenah, Wis. 54956. Meets twice a year, May and September.

Wyoming Radiological Society
Secretary, Dr. J. D. Grant, Memorial Hosp., Sheridan, Wyo. Meets in fall with State Medical Society and in spring on call of President.

Cuba, Mexico, Puerto Rico and Central America

Asociación Costariccense de Radiología
Secretary, Dr. Jorge Vargas Segura, Apartado 5367, San José, Costa Rica.

Asociación de Radiólogos de Centro America y Panamá. Comprising: Guatemala, El Salvador, Honduras, Nicaragua, Costa Rica and Panamá.
Secretary-General, Dr. Roberto Calderón, Calle Central Oeste No. 218, Managua, Nicaragua, Central America. Meets annually in a rotating manner in the six countries.

Sociedad de Radiología de El Salvador
Secretary, Dr. Julio Astacio, 5a Av. Nte. No. 434, San Salvador, Rep. El Salvador.

Sociedad de Radiología de Guatemala
Secretary, Dr. Carlos E. Escobar, 9ª. Calle A 0-05, Zona 1, Guatemala.

Sociedad de Radiología y Fisioterapía Cubana
Secretary, Dr. Miguel A. García Plasencia, Hospital Curie, 29 y F, Vedado, Habana, Cuba. Meets monthly at Curie Hospital.

Sociedad Mexicana de Radiología, A.C.
Coahuila No. 35, México 7, D. F.
Secretary-General, Dr. Ramón Ruenes.
Meets first Monday of each month.

Asociación Puertorriqueña de Radiología
Secretary, Dr. R. B. Díaz Bonnet, Suite 504, Professional Bldg., Santurce, Puerto Rico.

Sociedad Radiológica Panameña
Secretary, Dr. L. Arrieta Sánchez, Apartado No. 6323, Panamá, R. de P. Meets monthly in a department of radiology of a local hospital chosen at preceding meeting.

Sociedad Radiológica de Puerto Rico
Secretary, Dr. Felipe N. de Jesús, Apt. 9387, Santurce, Puerto Rico. Meets second Thursday of each month at 8:00 P.M. at the Puerto Rico Medical Association Bldg. in San Juan.

British Commonwealth of Nations

Association of Radiologists of the Province of Quebec
Secretary, Dr. R. Robillard, Notre-Dame Hospital, 1560 Sherbrooke St., East, Montreal, Que., Canada. Meets four times a year.

British Institute of Radiology
Honorary Secretary, Dr. G. H. du Boulay, 32 Welbeck St., London, W. 1, England. Meets monthly from October until May.

Canadian Association of Physicists, Division of Medical and Biological Physics.
Honorary Secretary-Treasurer, Paul M. Pfalzner, Department of Therapeutic Radiology, University of Western Ontario, London, Ontario, Canada.

Edmonton and District Radiological Society
Secretary, J. D. R. Miller, M.B., University of Alberta Hospital, Edmonton, Alberta, Canada. Meets third Thursday of each month October to May, except December, at various Edmonton Hospitals.

Faculty of Radiologists
Honorary Secretary, Dr. J. N. Pattinson, 47 Lincoln's Inn Fields, London, W.C.2, England.

Faculty of Radiologists, Royal College of Surgeons in Ireland
Registrar, Dr. H. O'Flanagan, F.R.C.P.I., D.P.H., 123 St. Stephens Green, Dublin 2, Ireland.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets third Friday each month at 4:45 P.M. at the Royal Society of Medicine, 1 Wimpole St., London, W. 1, England.

Canadian Association of Radiologists
Honorary Secretary-Treasurer, Dr. Maurice Dufresne, *Associate Honorary Secretary-Treasurer*, Dr. F. Robert MacDonald, 1555 Summerhill Ave., Montreal 25, Que., Canada. Annual Meeting at the Hotel Vancouver, Vancouver, B.C., March 10–14, 1969.

Montreal Radiological Study Club
Secretary, Dr. Leonard Rosenthall, Montreal General Hospital, Montreal, Que., Canada. Meets first Tuesday evening, October to April.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Société Canadienne-Française de Radiologie
Secretary General, Dr. Guy Duckett, 1385 est, rue Jean Talon, Montréal P.Q., Canada. Meets every third Tuesday from October to April. Annual Meeting: Nov. 13–15, 1969.

Toronto Radiological Society
Secretary, Dr. George Wortzman, Toronto General Hosp., Toronto 12, Ont., Canada. Meets second Monday of each month, September through May.

College of Radiologists of Australasia
Honorary Secretary, Dr. T. P. Loneragan, c/o British Medical Agency, 135 Macquarie St., Sydney, N.S.W., Australia.

South America

Asociación Argentina de Radiología
Secretary, Dr. Lidio G. Mosca, Avda. Gral. Paz 151, Córdoba, Argentina. Meetings held monthly.

Ateneo de Radiologia
Secretary, Dr. Victor A. Añaños, Instituto de Radiologia, Santa Fe 3100, Rosario, Argentina. Meets monthly on second and fourth Fridays at 7:00 P.M. in the Hospital Nacional de Centenario, Santa Fe 1300, Rosario.

Colégio Brasileiro de Radiologia
Secretary-General, Dr. Miguel Mario Céntola, Caixa Postal 5984, São Paulo, Brazil.

Sociedad Argentina de Radiologia
Secretary-General, Dr. Oswaldo E. Zerbo, Santa Fe 1171, Buenos Aires. Meetings are held monthly.

Sociedad Boliviana de Radiología
Secretary, Dr. Javier Prada Méndez. Casilla 1182, La Paz, Bolivia. Meets monthly. General assembly once every two years.

Sociedade Brasileira de Radiologia
Secretary, Dr. Armando Rocha Amoédo, Cxa Postal 1532, Rio de Janeiro, Brazil. General Assembly meets every two years in December.

Sociedade Brasileira de Radioterapia
Secretary, Dr. Oscar Rocha von Pfuhl, Av. Brigadeiro Luiz Antonio, 644, São Paulo, Brazil. Meets monthly on second Wednesday at 9:00 P.M. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

Sociedad Chilena de Radiología
Secretary, Dr. Manuel Concha, Casilla 13426, Santiago, Chile. Meets fourth Friday of each month.

Sociedad Colombiana de Radiologia
Secretary-General, Dr. Armando Uribe, Hospital Militar Central, Apartado aéreo No. 5804, Bogotá, Colombia. Meets last Thursday of each month.

Sociedad Ecuatoriana de Radiología y Fisioterapía
Secretary, Dr. Carlos Palau, Av. Bogotá 206, Guayaquil, Ecuador.

Sociedad Paraguaya de Radiología
Secretary, Dr. Miguel González Addone, 15 de Agosto 322, Asunción, Paraguay.

Sociedad Peruana de Radiologia
Secretary-General, Dra. Ladis Delpino, Instituto de Radiología "Cayetano Heredia" Hospital Arzobispo

Loayza, Lima, Perú. Meets monthly except during January, February and March.

SOCIEDAD DE RADIOLOGICA DEL ATLANTICO
Secretary, Dr. Raul Fernandez, Calle 40 #41–110, Baranquilla, Colombia. Society meets monthly at the Instituto de Radiología.

SOCIEDAD DE RADIOLOGÍA, CANCEROLOGÍA Y FÍSICA MÉDICA DEL URUGUAY
Secretary-General, Dr. José Claussius, Av. Agraciada 1464, piso 13, Montevideo, Uruguay.

SOCIEDADE DE RADIOLOGÍA DE PERNAMBUCO
Secretary, Dr. Manoel Medeiros, Instituto de Radiologia da Faculdade de Medicina da Universidade do Recife, Caixa Postal 505, Pernambuco, Brazil.

SOCIEDAD DE ROENTGENOLOGÍA Y MEDICINA NUCLEAR DE LA PROVINCIA DE CÓRDOBA
Secretary-General, Dr. Lucas C. Di Rienzo, Ave. Grl. Paz. 151, Córdoba, Argentina.

SOCIEDAD VENEZOLANA DE RADIOLOGÍA
Secretary-General, Dr. Modesto Rivero Gonzáles, Apartado No. 9362 Candelaria, Caracas, Venezuela. Meets monthly, third Friday at Colegio Médico del Distrito Federal, Caracas.

CONTINENTAL EUROPE

ÖSTERREICHISCHE RÖNTGEN-GESELLSCHAFT
President, Dr. Konrad Weiss, Mariannengasse 10, Vienna 9, Austria. Meets second Tuesday of each month in Allgemeine Poliklinik.

SOCIÉTÉ ROYALE BELGE DE RADIOLOGIE
General Secretary, Prof. Simon Masy, Louvain, Belgium. Meets in February, March, May, June, September, October, November and December.

SOCIÉTÉ EUROPÉENNE DE RADIOLOGIE PÉDIATRIQUE
Permanent Secretary, Dr. Jaques Sauvegrain, Hôpital des Enfants-Malades, 149, rue de Sèvres, Paris 15e, France.
General Secretary, Dr. H. Ludin, Department of Roentgenology, Basler Kinderspital, Basel, Switzerland. Annual meeting: Warsaw, Poland, May 22–24, 1969.
Secretary, Dr. Kasawery Rowinski, Zaklad Radiologii Pediatrycynej Akademii Medycznej, Marzalkowska 24, Warszawa, Poland.

SOCIÉTÉ FRANÇAISE D'ELECTRORADIOLOGIE MÉDICALE, and its branches: SOCIÉTÉ DU SUD-OUEST, DU LITTORAL MÉDITERRANÉEN, DU CENTRE ET DU LYONNAIS, DU NORD, DE L'OUEST, DE L'EST, ET D'ALGER ET D'AFRIQUE DU NORD. Central Society meets third Monday of each month, except during July, August and September, rue de Seine 12, Paris, France.
Secretary-General, Dr. Ch. Proux, 9 rue Daru Paris 8e, France.

ČESKOSLOVENSKÁ SPOLEČNOST PRO ROENTGENOLOGII A RADIOLOGII
Secretary, Dr. Robert Poch, Praha 12, Srobárova 50, Czechoslovakia. Meets monthly except during July, August and September. Annual general meeting.

DEUTSCHE RÖNTGENGESELLSCHAFT
President, Professor Dr. med. Hanno Poppe, Radiologische Univ.-Klinik, Gossler Str. 10, 34 Göttingen, Germany.

SOCIETÀ ITALIANA DI RADIOLOGIA MEDICA E DI MEDICINA NUCLEARE
Secretary, Dr. Ettore Conte, Ospedale Mauriziano Torino, Italy. Meets annually.

NEDERLANDSE VERENIGING VOOR RADIOLOGIE
Secretary, Dr. C. B. A. J. Puijlaert, Prof. Dondersstraat 73, Tilburg, Netherlands.

SCANDINAVIAN RADIOLOGICAL SOCIETY
Secretary-General, Dr. C. E. Unnérus, Professor, Hagalund-Tapiola, Havsvindsvägen 5 C., Finland. Annual meeting.

SOCIEDAD ESPAÑOLA DE RADIOLOGÍA Y ELECTROLOGÍA MÉDICAS Y MEDICINA NUCLEAR
Secretary, Juan Gomez Lopez, Villanueva, 11, Madrid 1. Meets every second Friday of each month, Oct. to June, inclusive, in Madrid.

SCHWEIZERISCHE GESELLSCHAFT FÜR RADIOLOGIE UND NUKLEARMEDIZIN (SOCIÉTÉ SUISSE DE RADIOLOGIE ET DE MÉDECINE NUCLÉAIRE)
Secretary, Dr. Max Hopf, Effingerstrasse 47, Bern, Switzerland.

ASIA

INDIAN RADIOLOGICAL ASSOCIATION
Secretary, Dr. R. F. Sethna, Navsari Building, Hornby Road, Bombay 1, India.

INDONESIAN RADIOLOGICAL SOCIETY
Secretary, Professor Sjahriar Rasad, Taman Tjut Mutiah I Diakarta, Indonesia

IRANIAN RADIOLOGICAL SOCIETY
Secretary, Dr. Issa Yaghmai, P.O. Box No. 14-1151, Teheran, Iran. The Society meets on the second Saturday of each month.

ABSTRACTS OF RADIOLOGICAL LITERATURE

INDEX TO ABSTRACTS

ROENTGEN DIAGNOSIS

HEAD

SCHNEIDER, C., PREVOT, H., JR., and TZONOS, T.: Scintigraphy with ^{203}Hg and ^{99m}Tc in the diagnosis of brain tumours 473
WOLLIN, D. G., BINNINGTON, V. I., and PARTINGTON, M. W.: Cloverleaf skull. 473

NECK AND CHEST

ZITTEL, R. X.: Congenital localized (lobar) emphysema: diagnosis and treatment 473
SHEPARD, F. M. *et al.*: Residual pulmonary findings in clinical hyaline-membrane disease 473
HOWES, J. M., PENNY, S. F., and CHAMBERLAIN, G. E.: A solitary pulmonary lesion due to Coccidioides immitis 474
MANKIEWICZ, E., HENDERSON, J. A. M., and BELAND, J. E.: Pulmonary coccidioidomycosis 474
POULOSE, K., REBA, R. C., and WAGNER, H. N., JR.: Characterization of the shape and location of perfusion defects in certain pulmonary diseases 474

ABDOMEN

GALLUZZI, S.: The radiologic appearance of gastropathy with giant plicae (Ménétrier's disease) 475
BONFIELD, R. E., MARTEL, W., and BATSAKIS, J. G.: The significance of small gastric filling defects 475
CASTOR, W. R.: Spontaneous perforation of the bowel in the newborn following exchange transfusion 476
VIGNOLINI, R., DE ALBERTIS, P., and PAGANO, C.: Roentgencinevideography: technique and a note on the dosimetric problem 476
MERLI, E., and ZUCCONI, A.: Radiologic findings in calculi of the choledochus 476
SMITHWICK, W., III, GERTNER, H. R., JR., and ZUIDEMA, G. D.: Injection of hypaque (sodium diatrizoate) in the management of abdominal stab wounds 476

GENITOURINARY SYSTEM

HAMILTON, C. R., JR., and TUMULTY, P. A.: Thrombosis of renal veins and inferior vena cava complicating lupus nephritis 477
HARROW, B. R.: Ureteral injuries recognized after gynecologic operations 477

SKELETAL SYSTEM

ROBICHON, J., and GERMAIN, J. P.: Pathogenesis of osteogenesis imperfecta 477
JELETZKY, T., and BOHATIRCHUK, F.: Some features of Paget's disease of bone studied by stain historadiography 478
CAMPBELL, C. J., PAPADEMETRIOU, T., and BONFIGLIO, M.: Melorheostosis: a report of the clinical, roentgenographic, and pathological findings in fourteen cases 478
DENT, C. E., ENGELBRECHT, H. E., and GODFREY, R. C.: Osteoporosis of lumbar vertebrae and calcification of abdominal aorta in women living in Durban 478
LAURENT, Y. *et al.*: Osteosarcoma in an irradiated child—a case report 479
DECLERCQ, A., DODINVAL, P., and PAQUOT, J. P.: A new observation of familial dyschondrosteosis 479
TURANO, L.: Modern research on primary hyperparathyroidism 479
EYRING, E. J., and EISENBERG, E.: Congenital hyperphosphatasia: a clinical, pathological, and biochemical study of two cases 480
STOREY, G. O.: Bone necrosis in joint disease 480
CLOUSE, M. E., AUFRANCE, O. E., and WEBER, A. L.: Roentgenologic and clinical evaluation of vitallium mold arthroplasty of the hip 481

BLOOD AND LYMPH SYSTEM

FLANC, C.: An experimental study of the recanalization of arterial and venous thrombi 481
JOHNER, C. H., and RANNIGER, K.: Mediastinal lymphography 482

RADIATION THERAPY

VON RONNEN, J. R.: Histological and radiographical classification of osteosarcoma in relation to therapy: a review of 245 cases located in the extremities 482
GOLDSTEIN, A. G., D'ESCRIVAN, J. C., and ALLEN, S. D.: Hemorrhagic radiation cystitis 482
HABECK, E. A., and PETERS, L. M.: Evisceration of bowel through the vagina following

irradiation for cervical carcinoma: report of first known case..... 483

RADIOISOTOPES

ASHBURN, W. L. *et al.*: Cerebrospinal fluid rhinorrhea studied with the gamma scintillation camera..... 483

JOHNS, D. G. *et al.*: ^{131}I-3′-iodoaminopterin: a gamma labeled active-site-directed enzyme inhibitor..... 484

WANEBO, C. K. *et al.*: Breast cancer after exposure to the atomic bombings of Hiroshima and Nagasaki..... 484

FRASER, F. C.: Genetic counselling and the physician..... 484

ROENTGEN DIAGNOSIS

Head

Schneider, C., Prevot, H., Jr., and Tzonos, T. Scintigraphy with ^{203}Hg and ^{99m}Tc in the diagnosis of brain tumours. *German Med. Monthly*, July, 1968, *13*, 309–314. (From: Division of Nuclear Medicine, Department of Radiology, Division of Neurosurgery and Department of Neurology, University of Hamburg, Hamburg, Germany.)

A review of typical scintigraphic findings in common primary intracranial tumors was made in 95 patients with Hg^{203} chlormerodrin and 419 examined with Tc^{99m}. In addition, 1,572 photoscintigrams were made.

With Hg^{203} chlormerodrin, meningiomas were characteristically outlined sharply and clearly, indicating intense accumulation of the mercury in the lesion. In the literature the detection rate is given as 95 per cent and in the authors' experience, using Hg^{203} chlormerodrin in 13 cases, none were missed. Gliomas were variable in the degree to which they took up labeled chlormerodrin. The glioblastoma detection rate varied from 80 to 90 per cent in collected statistics, but the astrocytomas showed a lower detection rate, between 55 and 70 per cent. The detection rate of posterior fossa tumors was around 50 per cent.

Technetium 99m is a radioisotope with a short half life. This plus its manner of distribution in the body results in a lower dose rate to the patient than Hg^{203} chlormerodrin, even with given doses 10 to 15 times greater. Consequently, tumor labeling is better and detection rate higher.

The site of a tumor can be demonstrated by either Tc^{99m} or Hg^{203}, with an over-all detection rate of 79 per cent for Hg^{203} and 85 per cent for Tc^{99m}. Gliomas of the cerebral hemisphere are detected slightly better by Tc^{99m} (92 per cent) than by Hg^{203} (81 per cent). Detection rate is influenced more by the site of the tumor than by its nature. For this reason, the possibility of misinterpretation of non-neoplastic lesions which give positive scintiscans must be considered.—*Lois Cowan Collins, M.D.*

Wollin, D. G., Binnington, V. I., and Partington, M. W. Cloverleaf skull. *J. Canad. A Radiologists*, Sept., 1968, *19*, 148–154. (From: Department of Radiology, Kingston General Hospital, Kingston, Ontario, Canada.)

Cloverleaf skull is a rare congenital deformity of the skull associated with mental retardation.

Two cases are reported. Pneumographic and angiographic studies were carried out on one who is, at the age of 8 years, the oldest reported living child with this rare condition.

It is suggested that the basic lesion is an abnormal synostosis of the cranial sutures.—*John H. Harris, M.D.*

Neck and Chest

Zittel, R. X. Congenital localized (lobar) emphysema: diagnosis and treatment. *German Med. Monthly*, Aug., 1968, *13*, 369–372. (From: The Department of Surgery, Freiburg University, Freiburg, Germany.)

Congenital "localized" or "lobar" emphysema is a rare disorder, mainly of infancy and early childhood. Respiratory troubles (dyspnea, spasmodic breathing, cyanosis, cough, recurrent bronchopulmonary infection) usually begin a few hours or days after birth and resist treatment. Their cause is an emphysematous overdistention of one lobe, more rarely of two lobes or of a whole lung, progressively displacing the mediastinum and the rest of the lungs.

While the pathogenesis is obscure, the condition is obviously congenital. Changes in the bronchi of the affected lobe, especially bronchiomalacia, have been found in nearly half the cases. The possible causes of emphysema which have been described in about one-third of reported cases are folds of bronchial mucosa, external compression of bronchi (as by vascular anomalies) and changes in alveolar structure.

Evaluation of 150 reported cases reveals that the left upper lobe was involved in over half the cases, with the right upper and middle lobes being much more rarely affected. The combination of left upper and right middle lobes seemed to be typical of the very rare bilateral involvement: for the whole of one lung to be involved was also very rare. In only one case was a lower lobe alone affected.

Roentgenographically, there is increased translucency of the involved portion of the lung, which, however, contains well-defined lung markings. There may be atelectasis of other portions of the same lung, and it is these areas that are usually affected by recurrent bronchopulmonary inflammation. Mechanical pressure from the "lobar" overdistention results in displacement of the heart and mediastinal structures to the opposite side, depression of the ipsilateral leaf of the diaphragm, and bulging or enlargement of that side of the thorax.

Differential diagnostic considerations include pulmonary cysts, obstructive emphysema following aspiration of a foreign body, bullous emphysema, pulmonary agenesis, pneumothorax, and diaphragmatic hernia with displacement of bowel into the thorax.

Resection of the affected lung segments is considered to be the only potentially successful treatment.—*Donald M. Monson, M.D.*

Shepard, Frank M., Johnston, Richard B., Jr., Klatte, Eugene C., Burko, Henry, and Stahlman, Mildred. Residual pulmonary findings in clinical hyaline-membrane disease. *New England J. Med.*, Nov. 14, 1968,

279, 1063–1071. (From: The Departments of Pediatrics and Radiology, Vanderbilt University School of Medicine, Nashville, Tenn. 37203.)

Seventy infants diagnosed clinically as having hyaline membrane disease with physical examination and chest roentgenograms were followed for 2 to 5 years. The object of the study was to determine the long-term sequelae of the disease—its frequency, origin, and relation to the clinical picture. All of the infants were initially treated with alkalizing agents, antibiotics, and oxygen. Nineteen of the 70 infants were clinically more severely ill and also received prolonged ventilatory assistance. On subsequent follow-up, 6 children from this "respirator group" had definitely abnormal roentgenograms. The findings consisted of increased parenchymal markings suggestive of pulmonary fibrosis, overexpansion of the lungs, and infiltrates. Clinically 2 of these children had recurrent bouts of wheezing and pulmonary infections.

The question is whether these findings are secondary to the primary disease process or to oxygen administration, respirator therapy, or infection.

The authors conclude that residual abnormal roentgenographic findings are related to the severity of the primary disease rather than to any specific factors such as ventilatory assistance or oxygen toxicity. This has yet to be resolved, however.—*Victor G. Mikity, M.D.*

Howes, J. M., Penny, Stuart F., and Chamberlain, George E. A solitary pulmonary lesion due to Coccidioides immitis. *Canad. M. A. J.*, Nov. 23, 1968, *99*, 1007–1008. (Address: Dr. J. M. Howes, 291 Ninth Street East, Owen Sound, Ontario, Canada.)

Coccidioidomycosis is rarely seen in Canada. In the literature, there have been only 3 cases reported.

The authors describe, with confirmation, the case of a 38 year old woman who had traveled a few months before admission to the hospital into Northern Mexico and Southern United States.

The tests and results of them are presented in detail.—*David C. Alftine, M.D.*

Mankiewicz, E., Henderson, J. A. M., and Beland, J. E. Pulmonary coccidioidomycosis. *Canad. M. A. J.*, Nov. 23, 1968, *99*, 1003–1006. (Address: Dr. E. Mankiewicz, Director of Laboratories, Royal Edward Chest Hospital, 3650 St. Urbain Street, Montreal 18, Quebec, Canada.)

Histoplasmosis recently has reached epidemic proportions in the Montreal region.

The present report entails a case of pulmonary coccidioidomycosis—a disease which is endemic in the warm dry Southwestern United States. It concerns a 27 year old white Canadian woman who made extensive camping trips in Southwestern United States and apparently acquired the disease in 1965. A chest lesion was discovered a few months later. This was removed by thoracotomy and found to be due to infection by *Coccidioides immitis*.—*David C. Alftine, M.D.*

Poulose, Kattadiyil, Reba, Richard C., and Wagner, Henry N., Jr. Characterization of the shape and location of perfusion defects in certain pulmonary diseases. *New England J. Med.*, Nov. 7, 1968, *279*, 1020–1025. (From: The Division of Nuclear Medicine, the Johns Hopkins Medical Institutions, Baltimore, Md. 21205.)

Lung scanning following intravenously injected radioactive particles is used as a method of diagnosing a variety of types of pulmonary abnormalities. In an attempt to determine the diagnostic reliability of the various types of scanning defects, scans were studied in 4 groups of patients: Group I consisted of 54 patients with clinical diagnosis of pulmonary embolism; Group II consisted of 52 patients with proved pulmonary tuberculosis; Group III consisted of 22 patients with chronic obstructive pulmonary disease; and Group IV consisted of 12 patients with proved carcinoma of the lung.

The term "concave" was used to describe a defect at the periphery of the lung that was concave in shape. Defects which appeared as a generalized diminution of perfusion were called "diffuse." Complete absence of blood flow to one or more zones (upper, middle, or lower) was referred to as "complete." A blunted costophrenic angle was considered a fourth type.

Concave defects occurred in 72 per cent of patients with pulmonary embolism, and in 33 per cent the defects were concave. These are comparable to the densities convex towards the heart which are seen on roentgen examination (Hampton's hump).

A diffuse type of defect was noted in 92 per cent of patients with pulmonary tuberculosis. The upper lungs were the most frequent sites of perfusion defects. Complete agreement between the frontal area of the lesion on the scan and on the roentgenogram was seen in 43 per cent. In 15 per cent, the scan area was larger, or smaller, respectively, than the roentgenologic evidence of involvement.

In patients with chronic obstructive lung disease, 77 per cent had diffuse lesions and 36 per cent had concave defects. Involvement was more severe in the upper lung fields. In 40 per cent abnormality was limited to one side, although unilateral emphysema is infrequent.

Of the 12 patients with carcinoma of the lung, 11 showed a complete absence of perfusion of one or more zones. In 1 case a concave defect was seen, but the possibility of tumor embolus or thromboemboli could not be excluded.—*Lois Cowan Collins, M.D.*

Abdomen

Galluzzi, S. Il quadro radiologico della gastropatia a pliche giganti (Malattia di Ménétrier). (The radiologic appearance of gastropathy with giant plicae [Ménétrier's disease].) *Radiol. med.*, 1968, *54*, 1–34. (Address: Dott. Prof. Sergio Galluzzi, Viale XXIV Maggio 25, Siena, Italy.)

Giant rugal hypertrophy of the stomach was first described in detail by Ménétrier in 1888, as a "polyadénome en nappe." However, before him Leudet (1847) had called this disease "hypertrophie polypiforme" and Brissaud in 1885 gave it the name of "polyadénome gastrique." Since that time many synonyms were used to describe this disease, such as: plaque-like gastric adenoma (Brams, 1924), giant hypertrophic gastritis (Maimon *et al.*, 1947), gastritis hypertrophica glandularis (Michalek, 1959), localized hypertrophied gastric glands (Gurman *et al.*, 1954), tumoral hypertrophy of gastric mucosa (Sherman *et al.*, 1955), villous gastropathy (Berti, 1961), and protein-losing gastro-enteropathy (Schwartz *et al.*, 1961).

The author, under the heading of giant hypertrophy of the gastric rugae, considers: (1) a diffuse rugal hyperplasia; and (2) a circumscribed rugal hyperplasia or Ménétrier's disease.

The main differences between the 2 forms are: (1) in the diffuse manifestation there is almost complete involvement of the gastric mucosa; the incidence is almost equal in both sexes; there is frequent dyspepsia; gastric hypersecretion and dystonia are always present; the roentgen findings are not pathognomonic and are easily demonstrated. (2) In the Ménétrier type, the area involved is the upper segment of the greater curvature of the body of the stomach; there is a greater incidence in the female sex (3:1); there are no definite symptoms related to the upper gastrointestinal tract; gastric hyposecretion is present; finally, the typical roentgen findings must be looked for with accuracy and in special views.

The anatomic picture is characterized by a redundancy of the gastric rugae which follow an irregular course, mostly with a circumvoluted pattern. This finding stands out quite clearly, surrounded as it is by the part of the gastric mucosa not involved by the pathologic process. Macroscopically, there is no difference in the color, plasticity and aspect of the surface between the normal and abnormal rugae. The thickening of the rugae is simply produced by a proliferation of the normal histologic components of the mucosa with a prevalence of the mucous glandular elements and edema of the submucosal layer. The glandular tubules are elongated and frequently dilated near the surface. There are no atypic cells or other abnormalities in the muscular layers.

The symptoms are not always related to the gastrointestinal tract and are usually secondary to the degree of achlorhydria, hypoproteinemia and anemia.

The roentgen findings are dealt with by the author in great detail. Fundamentally the diagnosis is based on: (1) the accentuation of the gastric rugae; (2) the gross "dental-like" appearance fo the greater curvature; (3) the presence of deep sulci between rugae; (4) the clear limits of the area involved; (5) the plasticity of the gastric walls; and (6) the evolution of the process, which is usually quite slow.

In the differential diagnosis, hypertrophic gastritis, the polyadenomas, gastric varices, and malignant neoplasms should be considered.—*A. F. Govoni, M.D.*

Bonfield, Robert E., Martel, William, and Batsakis, John G. The significance of small gastric filling defects. *Surg., Gynec. & Obst.*, Dec., 1968, *127*, 1231–1235. (From: The Departments of Radiology and Pathology, The University of Michigan, Ann Arbor, Mich.)

Patients in whom small gastric filling defects are demonstrated roentgenographically are often promptly subjected to surgical exploration. The au-

PATHOLOGIC ENTITIES ACCORDING TO SIZE AND NUMBER OF LESIONS IN 21 PATIENTS

Groups	No. of Instances
Group 1, solitary lesion, 1 cm. or less	
Retention polyp	1
Hyperplastic mucosal nodule	2
Adenoma	1
Carcinoid	1
Group 2, solitary lesion, 1.1 to 2 cm.	
Hamartoma	3
Inflammatory polyp	1
Adenoma	2
Adenocarcinoma	1
Group 3, solitary lesion, 2.1 to 3 cm.	
Hyperplastic mucosal nodule	1
Adenoma	1
Leiomyoma	1
Adenocarcinoma	1
Group 4, multiple lesions, up to 3 cm.	
Hyperplastic mucosal nodules	2
Adenomas*	3
Hamartomas	1
Inflammatory polyp	1
Total	23

* One patient with the Peutz-Jeghers syndrome in Group 4 had both adenomas and hamartomas and another patient in Group 4 had an inflammatory polyp as well as 2 adenomas.

Carcinoma *in situ* was found at the tip of 1 of 2 adenomatous polyps in 1 of these patients.

thors state that the wisdom of such management should be questioned, inasmuch as the great majority of these lesions are benign and may be of no clinical significance.

Patients were included in this study if the largest diameter of the gastric filling defect was 3 cm. or less, as measured on the roentgenogram.

At the University Hospital of Ann Arbor, Michigan, during the 10 year period from 1953 to 1963, 192 examples of relatively small polypoid lesions of the stomach were encountered, and the available roentgenograms of the involved patients were then reviewed. The roentgenographic examination of 21 of this group disclosed a lesion which fulfilled the size criterion.

The authors summarize by stating that small polypoid lesions of the stomach, particularly those 1 cm. or less in diameter and those that are pedunculated, are likely to be benign. The roentgenographic demonstration of such a lesion should not be considered as an absolute justification for exploratory laparotomy.—*C. Peter Truog, M.D.*

CASTOR, W. R. Spontaneous perforation of the bowel in the newborn following exchange transfusion. *Canad. M. A. J.*, Nov. 16, 1968, *99*, 934–939. (From: Department of Radiology, The General Hospital of Port Arthur, Port Arthur, Ontario, Canada.)

Two new cases of spontaneous neonatal pneumoperitoneum following exchange transfusions are discussed as to maturity, age, site of perforation, and survival of the infant. Five cases from the literature are also briefly considered.

The roentgenographic signs of free intraperitoneal air seen in supine, lateral decubitus, and upright roentgenograms are described. Prompt surgical intervention for repair of the perforation is stressed.

The most frequent location of the perforation involved the colon and terminal ileum. Enterocolitis and necrosis were noted at many of the sites of perforation during surgical exploration. Altered hemodynamics of portal venous flow subsequent to blood transfusions, causing mesenteric venous congestion, bowel infarction, and perforation of the bowel is submitted as an explanation for the spontaneous pneumoperitoneum.—*Victor G. Mikity, M.D.*

VIGNOLINI, R., DE ALBERTIS, P., and PAGANO, C. La roentgencinevideografia: tecnica e note sul problema dosimetrico. (Roentgencinevideography: technique and a note on the dosimetric problem.) *Radiol. med.*, 1968, *54*, 224–229. (Address: Dott. Prof. Renata Vignolini, Via G Acerbi, 6/7, Genova-Quarto, Italy.)

Using roentgencinevideography, the authors define that technique which permits them to cineradiograph the radiographic images transmitted by a telecamera on the television screen.

From an evaluation of the results obtained, the authors calculated that an examination of the gastrointestinal tract of a normo-type individual results in an exposure of 1.8 r by roentgencinevideography and of 14.8 r if cineradiography is used. This is explained by the fact that for the latter the technical factors range between 10–12 ma. and 80–100 kv., while the video technique requires only between 1–2 ma. and 85–90 kv.—*A. F. Govoni, M.D.*

MERLI, E., and ZUCCONI, A. Rilievi radiologici sulla calcolosi del coledoco. (Radiologic findings in calculi of the choledochus.) *Ann. radiol. diag.*, 1968, *40*, 233–261. (From: Istituto di Radiologia dell'Università di Genova and Reparto Radiologico Ospedale S. Giacomo, Novi Ligure, Italy.)

Calculi of the common bile duct are rather common, whether associated with cholelithiasis or as isolated pathologic phenomena.

The authors review the etiopathogenesis, the pathologic findings, the symptomatology, and in great detail, the roentgen investigations which better demonstrate the calculi of the common bile duct and the related findings.

It is felt that intravenous cholangiography associated with tomography should always be performed before any surgical intervention on the extrabiliary system is undertaken.—*A. F. Govoni, M.D.*

SMITHWICK, WALTER, III, GERTNER, HAROLD R., JR., and ZUIDEMA, GEORGE D. Injection of hypaque (sodium diatrizoate) in the management of abdominal stab wounds. *Surg., Gynec. & Obst.*, Dec., 1968, *127*, 1215–1224. (From: The Department of Surgery, The Johns Hopkins University School of Medicine and Hospital, Baltimore, Md.)

The authors state that at their hospital routine exploration by surgery in the management of abdominal stab wounds was carried out between the years 1955 to 1964. Forty per cent of the patients who underwent exploration had no peritoneal laceration. The technique of injection of hypaque into abdominal stab wounds was introduced in 1964 to reduce the number of patients who underwent exploration without peritoneal penetration.

Laparotomy is indicated without study with hypaque (sodium diatrizoate) in patients with unstable vital signs, obvious signs of intraperitoneal injury, such as protrusion of the intestine, omentum or abdominal rigidity, or signs of hemorrhage.

The technique is as follows: After the wound is cleaned, draped, and anesthetized, the tract, if large

enough, is probed with a finger. A large sized No. 16 to 18 French catheter is inserted into the wound, and a water-tight closure is established with the use of a purse-string suture of heavy silk. Two ampules, 60 cc., of sodium diatrizoate are then rapidly injected; the tube is clamped, and the skin is watched carefully for spillage around the catheter. Roentgenograms of the abdomen are made with the patient in flat, upright, and cross-table lateral positions.

One hundred and thirty-six injection studies were collected since 1965. Of the 136 injections, 45 were considered positive, 87 were considered negative, and 4 were considered nondiagnostic.

Of the 45 patients with positive studies, 44 underwent exploration and all had peritoneal lacerations.

Eighty-seven patients with negative examinations were reviewed. They were closely observed without exploration and had no significant morbidity. No deaths occurred in this group. There was one false negative study and one positive study was misinterpreted as negative. Four studies were considered nondiagnostic because the sodium diatrizoate entered the pleural cavity.

The authors consider this technique, as compared with other methods, to be definitely better and they conclude that careful application of this technique permits prompt, accurate, and efficient treatment of patients without an increased risk of morbidity or mortality.—*C. Peter Truog, M.D.*

GENITOURINARY SYSTEM

HAMILTON, CARLOS R., JR., and TUMULTY, PHILIP A. Thrombosis of renal veins and inferior vena cava complicating lupus nephritis. *J.A.M.A.*, Dec. 2, 1968, *206*, 2315–2317. (Address: Dr. P. A. Tumulty, 601 N. Broadway, Baltimore, Md. 21205.)

The nephrotic syndrome is a well recognized complication of renal involvement by systemic lupus erythematosus. Many of the clinical features of active lupus nephritis, including hematuria, proteinuria, and the nephrotic syndrome, however, are also found with renal vein thrombosis.

A 32 year old woman with typical clinical features of systemic lupus erythematosus suffered remissions and exacerbations of multiorgan involvement for 8 years. The development of massive lower extremity edema in addition to typical features of the nephrotic syndrome, raised clinical suspicion of inferior vena cava obstruction. This was confirmed by inferior vena cavagraphy which showed partial obstruction of the vena cava, paravertebral collaterals, intraluminal filling defects, and lack of renal vein "washout."

Renal vein thrombosis as a cause of the nephrotic syndrome is an established clinical entity. Although it may occur as an isolated phenomenon, thrombosis of the renal vein is more often associated with underlying renal disease. Etiologies include diabetic glomerulosclerosis, chronic glomerulonephritis, pyelonephritis, nephrosclerosis, renal cell carcinoma, and renal amyloidosis. This case adds lupus nephropathy to these background disorders. Pulmonary thromboembolism is a common finding in renal vein thrombosis, and when pulmonary emboli occur in association with the nephrotic syndrome, renal vein thrombosis should be suspected.

Renal biopsy may fail to differentiate the changes related to renal vein thrombosis from those produced by the underlying renal disease. The glomerular lesions may be identical to those of membranous glomerulonephritis, although in renal vein thrombosis alteration in the tubules and interstitial tissues is usually greater.—*Rosalind H. Troupin, M.D.*

HARROW, BENEDICT R. Ureteral injuries recognized after gynecologic operations. *Surg., Gynec. & Obst.*, Dec., 1968, *127*, 1267,–1273. (From: The Departments of Urology, Mercy and Cedars of Lebanon Hospitals, Miami, Fla.)

The close proximity of the ureter to gynecologic structures makes it a prime object for injury during an operation.

Actually, most unilateral ureteral injuries are not recognized until 1 or 2 weeks postoperatively. The author states that his experience includes 30 separate episodes during gynecologic operations in a 15 year period. Of 8 bilateral injuries, 6 were anuric and these unusual instances have already been reported or are to be published.

Excluding the 6 asymptomatic patients in whom ureteral injuries were recognized years later, the author has managed 16 with severe unilateral injuries, 13 being ureterovaginal fistulae, all of which followed nonradical operations.

The author describes his corrective surgical procedures.

In summary, he states that a few unilateral ureteral injuries may heal spontaneously or after ureteral catheter drainage. If conservative measures fail, reimplantation into the bladder using the Politano-Leadbetter procedure has been successful in almost all instances. Creation of a tunnel by using a bladder horn to the psoas muscle, if necessary, is most important to prevent reflux and subsequent pyelonephritis. In rare instances, transuretero-ureteral anastomosis can be employed.—*C. Peter Truog, M.D.*

SKELETAL SYSTEM

ROBICHON, J., and GERMAIN, J. P. Pathogenesis of osteogenesis imperfecta. *Canad. M. A. J.*, Nov. 23, 1968, *99*, 975–979. (Address: Dr. Jacques Robichon, 43 Bruyere Street, Ottawa, Ontario, Canada.)

Since 1849 the syndrome of fragility of bones, blue sclerae and otosclerosis has been known as osteogenesis imperfecta congenita when discovered in the fetus and newborn, and as osteogenesis imperfecta tarda when discovered in the adolescent and adult. It is agreed that the disease is transmitted as a dominant mendelian trait.

Many hypotheses are put forward as to the pathologic mechanisms which bring about the consequences of the disease.

This study is based upon examination of specimens from 20 patients, all under 16 years of age. The authors describe the methods of examinations of the specimens in detail and draw certain conclusions.

The most important conclusion is that osteogenesis imperfecta is characterized by a generalized increase in the number of osteocytes, while at some period in the evolution of the disease, increase in resorption and immaturity of architecture are noted.

The view is expressed that the pathogenesis of osteogenesis imperfecta is a biphasic process of resorption, one latent and one active. Thus, osteogenesis imperfecta could well be considered as a disease of increased bone resorption, rather than one of decreased bone formation.—*David C. Alftine, M.D.*

Jeletzky, T., and Bohatirchuk, F. Some features of Paget's disease of bone studied by stain historadiography. *J. Canad. A. Radiologists*, Mar., 1968, *19*, 25–33. (From: Department of Anatomy, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada.)

The bone changes in Paget's disease were studied by thin sections (10μ) of undecalcified bone using staining and historadiographic methods.

This is a highly technical article and will be of interest to students of bone absorption and regeneration.

In the summary the authors state that 2 features were particularly investigated:

A. Osteogenesis in the fibrovascular tissue; and
B. morphology of mosaic lines and the interrelation between their calcium content and the image in historadiograph and stained specimens.

Many reproductions of the stained specimens and historadiographs accompany the article.—*John H. Harris, M.D.*

Campbell, Crawford J., Papademetriou, Theodore, and Bonfiglio, Michael. Melorheostosis: a report of the clinical, roentgenographic, and pathological findings in fourteen cases. *J. Bone & Joint Surg.*, Oct., 1968, *50A*, 1281–1304. (Address: Dr. C. J. Campbell, Albany Medical College, Albany, N. Y. 12208.)

Fourteen previously unreported cases of melorheostosis are presented. The disease progressed rapidly in children and slowly in adults. Contracture and deformity were the earliest findings at birth or in early childhood and pain with stiffness in affected joints was the most common complaint in adult life. Soft tissue contractures and deformities, especially in the hands and feet, were usually found and treated before roentgenograms demonstrated the characteristic hyperostosis.

Roentgenograms made in infancy or early childhood usually showed a faint linear hyperostosis which was difficult to diagnose. This rapidly increased in the immature skeleton and more slowly in the adult skeleton, eventually producing the appearance of bone flowing along the cortex. The roentgenographic appearance was characterized by an irregular linear radiopacity along the major axis of long bones and there was usually a distinct border between the pathologic and normal bone. The linear hyperostosis extended along the limb, from one bone to the next and continued to the carpus or the tarsus as far as the phalanges. When two long bones (tibia and fibula or radius and ulna) lie parallel, usually only one was involved but occasionally the adjacent margins of two bones were affected. Abnormal osseous tissue was occasionally found in the periarticular soft tissues of some of the major joints such as the hip, knee, ankle, or shoulder.

Since the abnormality of the soft tissues of mesodermal origin, as manifested by contractures, was usually discovered earlier than the underlying hyperostosis, this often led to incorrect diagnoses. These abnormalities usually caused greater deformity and disability than the disease in the bone itself.

The pattern of involvement suggests that this disorder is a congenital abnormality akin to paraxial hemimelia and that it is initiated in embryonic life prior to the formation of the limb buds, but the spinal column, skull, and ribs may also be involved.—*E. Nicholas Sargent, M.D.*

Dent, C. E., Engelbrecht, H. E., and Godfrey, R. C. Osteoporosis of lumbar vertebrae and calcification of abdominal aorta in women living in Durban. *Brit. M. J.*, Oct. 12, 1968, *2*, 76–79. (Address: Dr. C. E. Dent, Professor of Human Metabolism, University College Hospital Medical School, London W.C.1., England.)

This study was made to determine the relationship of osteoporosis in old age and mechanical stress and muscular activity during early life; an incidental observation was the amount of calcification in the walls of the abdominal aorta.

Three groups of women, age 50–90 years, having different living habits were studied by means of lateral roentgenograms of the lumbar spine. One group of Bantu women were accustomed to heavy manual labor—including carrying great weights on

their heads; the second group was from the same rural area but had moved to Durban; the third group were white women living in Durban.

The findings indicate a much lower incidence of osteoporosis in the 2 groups of Bantu women than in the white women. The cause of the difference may be due to the social and dietary differences between the Bantu and the white women, rather than to muscular activity.

There was no correlation between the amount of calcification in the abdominal aorta and the osteoporosis.—*John H. Harris, M.D.*

Laurent, Y., Dextroux, J., Lebrun, J., and Rosillon, J. L'osteosarcome de l'enfant irradié: presentation d'un cas. (Osteosarcoma in an irradiated child—a case report.) *J. belge de radiol.*, 1968, *51*, 112–116. (Address: Dr. Y. Laurent, 186, Avenue Messidor Bruxelles 18, Belgium.)

The carcinogenic action of gamma radiation on bone has been known for quite some time. A review of the literature reveals several reports of bone sarcoma developing following radiation therapy of a soft tissue tumor, with unavoidable irradiation of adjacent bone structure, or of planned irradiation of bone because of a benign lesion or inflammatory disease. Thus in the management of such benign lesions the remedy may prove to be worse than the disease. The incidence of osteosarcoma, however, remains less than 1 per cent of treated cases.

Listed among the conditions that may be treated with radiation therapy are benign tumors of bone, especially giant cell tumors, inflammatory disease such as tuberculosis (no longer advocated or done at present). Osteogenic sarcoma, developing from incidental irradiation of bone during the treatment of benign and malignant disease of soft tissue, has occurred following treatment of angiomas and Wilms' tumor.

The authors report the case of a girl, born April 1950, who had an extensive angioma in the left axilla. At the age of 4 months she was treated with a 30 mg. radium mold for 20 hours, and at the age of 4 years received 4,250 r to the left axilla with an apparent good result. Normal growth and development followed. At the age of 16 years she complained of pain in the left arm aggravated by abduction and by palpation of the proximal humerus. Roentgenographic examination revealed structural irregularity of the proximal left humerus, presenting a moth eaten appearance and destruction of the cortex at the medial aspect. Biopsy confirmed the diagnosis of osteogenic sarcoma.

Using telecobalt 60 therapy a tumor dose of 6,000 r was delivered. Despite initial regression of the tumor, a chest roentgenogram made 1 month after completion of therapy revealed widespread hematogeneous nodular metastases in the lungs. At this point all attempts at curative therapy were abandoned.

The authors advise against radiation therapy of benign lesions, but fail to comment on the massive dose used.

Reproductions of 2 roentgenograms and 1 photomicrograph of the tissue biopsy accompany this case report.—*William H. Shehadi, M.D.*

Declercq, A., Dodinval, P., and Paquot, J. P. Une nouvelle observation familiale de dyschondrostéose. (A new observation of familial dyschondrosteosis.) *J. belge de radiol.*, 1968, *51*, 117–121. (Address: Dr. A. Declercq, Service de Radiologie, Hôpital de Bavière, Liège, Belgium.)

Dyschondrosteosis is characterized by moderate dwarfism, and shortening of the mid segments of the forearms and legs, with a Madelung type deformity of the forearm. Based upon the appearance of the forearms alone, the diagnosis of Madelung's deformity may be made without recognition of the malformation.

The authors report the case of a mother and one of her two daughters, on whom, because of the deformity of the forearm, the initial diagnosis of Madelung's deformity rather than dyschondrosteosis was made. The second daughter showed no evidence of any congenital malformation.

Since her childhood the mother was known to have a deformity of the forearm. At the age of 18 years she gave birth to her first daughter who was perfectly normal. At the age of 20 years she gave birth to her second daughter who presented the same abnormality the mother had.

Both mother and the second daughter were short, and had bilateral dorsal subluxation of the distal ulna. Roentgenologic examination revealed bilateral posterior and lateral curvature of the radial shaft with resultant widening of the interosseous space, posterior dislocation of the ulna at the distal radioulnar articulation, obliquity of the articulating surface of the distal radius, ogival deformity of the arch formed by the first row of carpal bones, with the semilunar bone projecting abnormally high. In addition, the mother had shortening of the radius and ulna, tibia and fibula, of both forearms and legs, and bilateral humerus vareus. The structure of the lateral tibial plateau was massive and was accompanied by lateral exostoses. The daughter presented essentially the same skeletal malformations.

Three tables of skeletal measurements and reproductions of 2 photographs and 3 skeletal roentgenograms accompany this article.—*William H. Shehadi. M.D.*

Turano, L. Recherches modernes sur l'hyperparathyroïdie primaire. (Modern research on primary hyperparathyroidism.) *J. belge de radiol.*, 1968, *51*, 180–187. (Address: Direc-

teur de l'Institut de Radiologie de l'Université de Rome, Italie.)

Primary hyperparathyroidism may be due to the presence of a functioning adenoma or to hyperplasia of the parathyroid gland.

The author refers to his previous work and to his several presentations on the subject. The clinical manifestations may occur in the form of: (1) renal involvement, with the occurrence of bilateral or unilateral opaque calculi, without skeletal lesions; (2) skeletal involvement, without renal calculi; and (3) renal and skeletal involvement.

Other clinical manifestations which may occur are duodenal ulcer, muscular weakness, nervous and cardiac conditions.

The author's recent investigation has been primarily concerned with: (1) the study of the histopathology of the fibro-osseous lesions by means of historadiography; and (2) the determination of the presence, location and size of a parathyroid adenoma by means of scintigraphy using Se^{75} methionine.

Involvement of the bony skeleton occurs in the form of fibrocystic osteitis as well as osteomalacia. The latter often results in a decrease in height, up to 10 cm. as observed in one of the author's patients, and in multiple fractures.

The author reports the cases of 3 female patients, ages 47, 62 and 52 years, respectively, with widely distributed fibrocystic osteitis. Renal calculi were present in the first two patients, while in the third patient calcarious precipitation in the renal parenchyma was found at autopsy. The presence of a large primary parathyroid adenoma, diagnosed by scintigraphy was surgically confirmed in the first two patients and at autopsy in the third patient.

The author's careful studies of bone structure by means of historadiography leads to the conclusion that in addition to the presence of fibrocystic osteitis, osteomalacia is a significant structural change in this disease. This is characterized by an abundant new formation of defective osteoid tissue which fails to calcify and which remains so until the process of healing sets in.

Nineteen reproductions of roentgenograms, historadiographs of bone sections, scintiscans and photographs of the removed parathyroid adenomas accompany this article.—*William H. Shehadi, M.D.*

EYRING, EDWARD J., and EISENBERG, EUGENE. Congenital hyperphosphatasia: a clinical, pathological, and biochemical study of two cases. *J. Bone & Joint Surg.*, Sept., 1968, *50A*, 1099–1117. (From: The Departments of Orthopaedic Surgery and Medicine, University of California School of Medicine, San Francisco, California, and Shriners' Hospital, Honolulu, Hawaii.)

Two siblings are reported with excessive fragility of their bones. They both appeared normal at birth, but after a few months exhibited progressive deformities. These included dwarfism, large heads, saddle noses, early loss of deciduous teeth, pigeon breasts, and bowed extremities with compensatory joint contractures. These were associated with blue sclerae, high frequency hearing loss, and generalized tenderness.

Roentgenographically, the skeleton appeared nearly normal early, but there was progressive generalized conversion to coarsely trabeculated, radiolucent bone. Subperiosteal layers of new bone formed on concave surfaces, which greatly increased the width of the long bones. There was associated diaphyseal bowing, but relatively normal epiphyses.

Blood chemistries revealed a normal calcium and phosphorus. Alkaline phosphatase was normal early, but with growth rose to very high levels and then dropped gradually. There were also elevated acid phosphatase and leucine amino peptidase activities.

In the urine there was heavy excretion of hydroxyproline peptide and hyperuricosuria. There was normal excretion and tubular resorption of phosphate.

The dynamics of bone remodeling indicated an extraordinarily rapid turnover of subperiosteal bone.

There was no evidence of a chromosomal defect and it was felt that the disease is probably autosomal recessive in character. The name congenital hyperphosphatasia was selected in preference over other descriptive terms, probably for the same condition, such as the wide bone type of osteogenesis imperfecta, hyperostosis corticalis deformans juvenilis, osteitis deformans in children, and familial osteoectasia with macrocranium.

The two siblings, a boy and girl, were studied exhaustively in a metabolic unit, and while the original article details the numerous specific findings and laboratory values, only pertinent general positive findings are summarized above.—*Donald M. Monson, M.D.*

STOREY, G. O. Bone necrosis in joint disease. *Proc. Roy. Soc. Med.*, Oct., 1968, *61*, 961–969. (From: Hackney Hospital, London, England.)

The term "necrosis" is used by the author to cover aseptic or avascular necrosis involving destructive changes in joints, although necrosis may not be the primary pathologic process. Septic necrosis, neoplastic, or other infiltrations may have to be considered in making the diagnosis, and indeed biopsy is often advisable. The various conditions described are summarized in the following table:

Bone "necrosis" in joint disease: classification

(1) Idiopathic avascular necrosis of the femoral head in adults
Perthes' disease

(2) Secondary avascular necrosis
Diffuse lupus erythematosus

Hemoglobinopathies
Decompression syndrome
Endocarditis
Local trauma (fracture, surgery)
Giant cell arteritis
Pancreatitis
Gaucher's disease
Multiple injuries, burns
Pregnancy
Hypercorticism
Angiokeratoma corporis diffusum
Radiation
Steroid arthropathy
Hyperuricemia
Alcoholism

Arthropathies in which "necrosis" may occur
(3) Rheumatoid arthritis, psoriatic arthritis
(4) Osteoarthrosis
(5) Charcot joints

The author limits his discussion to diseases of the hip. He concludes that the group of cases in which actual collapse of the hip occurs appears to represent a variation or complication of degenerative joint disease, although similar changes may result from rheumatoid arthritis. The collapse results either from avascular necrosis or from a condition related to senile osteoporosis causing attrition necrosis, but both processes may coexist. At the same time there are also some similarities to the Charcot joint.

It seems possible to trace the course of events roentgenologically, the early change being osteoporosis and sometimes areas of fluffy osteosclerosis with cystic changes in the femoral head. Later the bone takes on a firmer outline and the joint space seems to reform (possibly occupied by fibrocartilage). It is necessary to emphasize that care must be taken interpreting the roentgenograms in terms of pathology. The roentgen appearance alone also may be misleading, as in some patients the early changes do not always proceed to destruction of the femoral head. There seems to be no way of predicting the actual extent of destruction in the early cases.—*E. Nicholas Sargent, M.D.*

Clouse, Melvin E., Aufrance, Otto E., and Weber, Alfred L. Roentgenologic and clinical evaluation of vitallium mold arthroplasty of the hip. *Surg., Gynec. & Obst.*, Nov., 1968, *127*, 1042–1050. (From: The Departments of Radiology and Orthopedic Surgery, Harvard Medical School and Massachusetts General Hospital, Boston, Mass.)

Vitallium cup arthroplasty is utilized to interpose a durable surface between the bone of the acetabulum and the head, neck or shaft of the femur. If successful, a functioning joint is created. About 5,000 of these procedures have been performed at the Massachusetts General Hospital.

The procedure has been useful in various conditions, including congenital dislocation of the hip and Legg-Perthes' disease, ankylosis from previous infection or surgery, rheumatoid or degenerative arthritis, and recent or old fractures of the acetabulum.

The surgical indication depends upon the underlying condition.

Roentgenographic evaluation requires frontal and frog-leg views and assists in determining what operative procedure will be required.

Postoperatively, roentgenograms establish whether or not the cup remains in normal position and are helpful in demonstrating some of the complications occurring following surgery.

In a satisfactory arthroplasty, the apex of the newly formed acetabular dome should be 1.5 cm. superior and 1 to 2 cm. medial to the lateral rim of the acetabulum; the line of weight-bearing should be approximately 1.5 cm. medial to the lateral rim of the acetabulum or perpendicular to the anteroinferior iliac spine. The mold should project beyond the acetabular rim and not lock on the greater trochanter. Occasionally roentgenograms in abduction are helpful in demonstrating the range of motion at the site of surgery.

The authors point out that the roentgenographic appearance does not necessarily correlate with the clinical evaluation of the patient. Hip motion and function may be good despite a roentgenogram which suggests that it might not be.—*George L. Sackett, M.D.*

Blood and Lymph System

Flanc, Charles. An experimental study of the recanalization of arterial and venous thrombi. *Brit. J. Surg.*, July, 1968, *55*, 519–524. (From: Department of Surgery, King's College Hospital Medical School, London, S.E.5., England.)

The behavior of a thrombus in a vein is significantly different from the behavior of a thrombus in an artery. A thrombus in a vein usually recanalizes to such an extent that a patent lumen is restored, but in an artery a thrombus usually results in permanent occlusion. Therefore, it is clinically important to determine the factors which account for the difference of behavior of the thrombi.

Experiments were conducted in mongrel dogs (104 procedures in 62 dogs) to determine the effect of venous pressure and arterial pressure on thrombi in veins and arteries respectively, and also the effect of arterial pressure on thrombi in veins. To accomplish the latter, arteriovenous fistulas were produced distal to thrombi in the femoral veins of 8 dogs. The results were in accord with previous observations cited above. However, venous thrombi subjected to arterial pressure failed to recanalize effectively, suggesting that the pressure may be the significant factor in the difference in behavior of the thrombi in arteries

and veins, and the paradoxical behavior in veins grafted into arteries.

Another hypothesis suggested is that the venous endothelium is a richer source of fibrinolytic enzymes than the arterial endothelium, and that subjecting the wall of the vein to arterial pressure diminishes the fibrinolytic activity of the vein wall. In these experiments, 4 veins subjected to arterial pressure showed thickening of the wall and an increase in elastic fibers.—*Lois Cowan Collins, M.D.*

JOHNER, CARL H., and RANNIGER, KLAUS. Mediastinal lymphography. *Surg., Gynec. & Obst.*, Dec., 1968, *127*, 1313–1316. (From: The Departments of Surgery [Otolaryngology] and Radiology, University of Chicago, School of Medicine, Chicago, Ill.)

Metastatic spread of cancer of the head and neck to the mediastinum is a common clinical problem and raises the question of lymphatic pathways between these areas. The presence of direct communications between the lymphatic system of the head and neck and those of the mediastinum has been previously postulated.

This animal experiment was undertaken in an attempt to demonstrate such intercommunications. Mediastinoscopy provided access to mediastinal lymph nodes in 12 dogs. A small needle was then placed in the center of such a lymph node and iodized oil was slowly injected. Oblique roentgenograms of the chest were taken at intervals after the beginning of the injection. Extravasations occurred readily and good studies were obtained only in 6 dogs. Roentgenograms demonstrated lymphatic channels connecting bronchiomediastinal lymph nodes with the area of the jugulosubclavian venous angle at the root of the neck. Direct pathways between mediastinal and deep cervical lymphatics were not demonstrated. In 3 additional dogs similar injections were made into mid and deep cervical lymph nodes. No channels could be demonstrated leading to the mediastinum.

The authors point out, however, that establishment of new lymphatic pathways may result from interference with normal lymph flow by tumor or infection.—*Rosalind H. Troupin, M.D.*

RADIATION THERAPY

VON RONNEN, J. R. Histological and radiographical classification of osteosarcoma in relation to therapy: a review of 245 cases located in the extremities. (Leiden, The Netherlands.) *J. belge de radiol.*, 1968, *51*, 215–221.

Out of 311 cases of osteosarcoma in the files of the Netherlands Committee for Bone Tumours, 245 osteosarcomas located in the limbs were selected; 142 were treated 5 or more years previously, and in these cases the 5 year survival appears to be 20 per cent. In order to prevent useless mutilating operative procedures and in order to select those cases in which metastases may not yet have developed, a selection scheme derived retrospectively from characteristics of osteosarcomas in patients with long-term survival was devised. The selection was based both on histologic characteristics and radiographic findings.

On histologic grounds alone, the Netherlands Committee for Bone Tumours adopted the rule that for osteosarcomas of the fibrosarcomatous type or of the type with a low mitotic index, immediate amputation or exarticulation is advised. The results indicated that in these two groups the number of useless mutilating operative procedures was low. On the other hand, other histologic groups (*i.e.*, teleangiectatic types and variant forms) showed no distinctly favorable prospects and are not suitable for radical surgery.

However, among the osteosarcomas not belonging to the fibrosarcomatous type, or the type with low mitotic index, there remained a small number of cases showing a long survival time. The author, therefore, felt that it should be possible to select these cases for immediate radical surgery on a basis of characteristics also to be found in the radiologic picture rather than the histologic picture alone. Several distinct types could be distinguished and classified in this group. These are the "normal type," "cystic type," "osteosclerotic type," "periosteal type," and "variants." He found that in 9 cases where the combination of histologically "normal type" with what might be called radiologically the periosteal type existed, a distinctly longer survival could be observed. Therefore, although the numbers are small, in these cases immediate radical surgical treatment should be seriously considered, in the author's opinion.

The other radiologic types showed no distinct indications for a more favorable prognosis. For these patients with an osteosarcoma in which a poor prognosis can be expected, the Netherlands Committee for Bone Tumours advises: irradiation with a tumor dose of 6,000–7,000 rads over 6–7 weeks, a 6 month waiting period, and then, if no metastases are demonstrable, amputation or exarticulation.—*E. Nicholas Sargent, M.D.*

GOLDSTEIN, ARTHUR G., d'ESCRIVAN, JULIO C., and ALLEN, SAMUEL D. Hemorrhagic radiation cystitis. *J. Urol.*, Aug., 1968, *40*, 475–478. (Address: Dr. Arthur G. Goldstein, Burlington County Memorial Hospital, Mount Holly, N. J.)

Although microscopic or even gross hematuria following radiation therapy to the pelvis is not unusual, severe vesicle hemorrhage is, fortunately, less common. Radiation cystitis may occur at any time from months to 14 years after completion of the radiation therapy. Pathologically, the mucosa

atrophies and becomes thin, pale, and inelastic, while marked fibrosis and capillary dilatation occur in the submucosa. Necrotising arteriolitis results in impaired contractility of the vessels as the musculature of the arterioles is replaced by fibrous tissue. The altered bladder vasculature is fragile, and can be the source of recurrent profuse hemorrhage.

Radiation-induced bladder injuries occur more often in patients with underlying bladder disease when higher doses of radiation are given. Hematuria most frequently follows intracavitary radiation therapy, and is unusual after supervoltage therapy. Radiation cystitis has also been reported due to cyclophosphamide.

Cystoscopically, the mucosa is pale and edematous. The vessels may appear as petechiae, telangiectases, or dilated and tortuous channels. Ulcerated and encrusted lesions may be present. Typical of the 4 reported cases by the authors was the lack of specific bleeding points, while fresh blood accumulated in the bladder. If a specific lesion does exist, biopsy will distinguish recurrent neoplasm from radiation reaction, although such procedure may precipitate brisk bleeding.

The initial treatment of hemorrhagic radiation cystitis requiring multiple blood transfusions should be conservative, and include the following adjuncts: There must be adequate blood replacement; cortisone derivatives (prednisone), and tocopherol (Vitamin E) may be tried, although the latter is of questionable value. Constant bladder irrigations with silver nitrate (in solution stronger than 1:5,000) may be tried if frequent clot retention occurs or previously employed drugs are unsuccessful. Fulguration may be used in cases where a specific bleeding point is noted, and there has to be appropriate chemotherapy. Experimental evidence has indicated that direct electric current hemostasis may be useful.

Certainly, a trial of conservative therapy is warranted, as in one reported series of 30 patients with gross hematuria from radiation cystitis, the bleeding recurred in only 3 cases. A decision as to when to operate is difficult, especially in those cases where the bleeding is intermittent. Once stopped, it may never recur, but if it does recur, the patient is usually not an optimal risk. Each case must be considered individually. If conservative therapy fails, supravesical urinary diversion and bilateral hypogastric artery ligation are indicated. Cystectomy at this time should be performed only if the patient's condition permits. If urinary diversion and hypogastric artery ligation alone do not adequately control the bleeding, secondary cystectomy becomes necessary. —*Donald M. Monson, M.D.*

Habeck, Edgar A., and Peters, Leo M. Evisceration of bowel through the vagina following irradiation for cervical carcinoma: report of first known case. *Wisconsin M. J.*, Aug., 1968, *67*, 374–375. (Address: Dr. Edgar A. Habeck, 5631 West Lincoln Avenue, Milwaukee, Wis. 53219.)

The authors report a case of a 49 year old woman who was found to have a squamous cell carcinoma of the cervix, Stage II. This was treated with an Ernst applicator with a dose of 3078.5 mg. hr. and 16 days later an additional dose of 1818.0 mg. hr. Twelve days later external cobalt therapy was administered over a period of 32 days.

Examination 6 weeks after completion of treatment revealed a normal postirradiation appearance.

She was followed and had a normal course until 6 years later when she was straining at stool at home and about 18 inches of small bowel eviscerated through the vagina. Manual reduction was easily accomplished by elevating the pelvis. She was transferred to the hospital and maintained in the Trendelenburg position in bed, and a liquid diet with penicillin therapy was started. No peritonitis developed. Cytology studies were negative.

A high posterior colporrhaphy and partial vaginectomy were performed and the patient made an uneventful postoperative recovery.

This is the first reported case of this complication of radiation therapy.—*George L. Sackett, M.D.*

RADIOISOTOPES

Ashburn, William L., Harbert, John C., Briner, William H., and di Chiro, Giovanni. Cerebrospinal fluid rhinorrhea studied with the gamma scintillation camera. *N. M. J. Nuclear Med.*, Oct., 1968, *9*, 523–529. (From: The National Institutes of Health, Bethesda, Md.)

Cerebrospinal rhinorrhea is a much feared complication of head injuries, and its diagnosis is exceedingly difficult. Even more difficult is identifying the exact site of a leak before exploratory craniotomy.

The authors have approached the problem by means of radioisotope cisternography, in which 100 μc of high specific activity I^{131}-labeled human serum albumin (HSA) is injected into the lumbar subarachnoid space. Serial rectilinear scans of the head are then made to visualize the normal flow of spinal fluid, or any alteration in its flow dynamics. The authors have also prepared, and used, high specific activity Tc^{99m} HSA, which they have employed in tracer doses of 2 mc. They feel that this latter agent is the tracer of choice.

Diffusion of the tracer agent is followed with scintiphotos made with an Anger camera at 1, 3 and 24 hours after administration. Various normal patterns are illustrated, as are the patterns to be anticipated when a leakage site is identified in a case of true rhinorrhea.

The authors' detailed experience with 14 cases of suspected rhinorrhea is given in detail, and shows a

generally good agreement between cysternographic diagnosis and surgical confirmation. The method is a useful one in the diagnosis of this often obscure entity.—*Frederick J. Bonte, M.D.*

JOHNS, DAVID G., SPENCER, RICHARD P., CHANG, PAULINE K., and BERTINO, JOSEPH R. ^{131}I-3′-iodoaminopterin: a gamma labeled active-site-directed enzyme inhibitor. *N. M. J. Nuclear Med.*, Oct., 1968, *9*, 530–536. (From: Yale University School of Medicine, New Haven, Conn.)

The authors were interested in ascertaining the *in vivo* binding and distribution of the folate antagonists, aminopterin and methotrexate. They are known to bind to the active site of the enzyme dihydrofolate reductase, with a rather high affinity.

Employing the method of Loo the authors synthesized 3′-iodoaminopterin, which is described in detail in this paper. The subjects of the study were patients who were to receive folate antagonists in the course of their treatment for head and neck tumors or lymphomas. A tracer dose of 150–200 μc was used in each patient. Blood samples were taken at intervals after the intravenous administration of I^{131}-labeled 3′-iodoaminopterin, and the organ distribution was determined by 1 minute counts over liver, spleen, thyroid, kidneys, sacrum and the skeletal muscle of the right thigh at intervals after administration. Regional scans were performed at 4 and 24 hours after the initial injection.

Early after injection the largest fraction of radioactivity was detected over the liver and kidneys. Thereafter, the distribution was complicated by the fact that deiodination occurs *in vivo*. In addition to the sites described above, considerable activity was detected over the sternal bone marrow. The presence of tracer in these sites is no doubt due to specifically high concentrations of dihydrofolate reductase. A high concentration was also obtained in the thyroid gland, and it could be prevented by blocking with iodide. This is additional evidence of *in vivo* deiodination of the tracer agent.—*Frederick J. Bonte, M.D.*

WANEBO, C. K., JOHNSON, K. G., SATO, K., and THORSLUND, T. W. Breast cancer after exposure to the atomic bombings of Hiroshima and Nagasaki. *New England J. Med.*, Sept. 26, 1968, *279*, 667–671. (From: The Atomic Bomb Casualty Commission, Hiroshima and Nagasaki, Japan.)

Although mammary cancer was known to develop in certain strains of mice after whole body exposure to ionizing radiation, only recently has it been recognized that there might be an increased incidence of this neoplasm in irradiated women. Of particular interest is an observation that there is a higher incidence of breast cancer in women who underwent many chest fluoroscopic examinations in the course of management of pulmonary tuberculosis with artificial pneumothorax.

The survivors of the Hiroshima and Nagasaki bombings were examined at the clinics of the Atomic Bomb Casualty Commission. The subjects were 10,357 survivors and they were studied by biennial physical examination, chest roentgenograms, electrocardiograms and various laboratory procedures. Parallel efforts were made to ascertain individual radiation exposure.

The study has disclosed that 31 women have developed breast cancer since 1945. The dose determinations are inexact for 4 of these women, but 13 of the remaining 27 can be presumed to have received 90 or more rads of chest or whole body exposure. The average interval from exposure to detection of disease was 14.7 years.

The authors believe that the incidence of breast cancer in the women in this series is higher than that in a comparable group of the Japanese population, and that the onset of cancer occurs at an earlier age in the study group than in the general population. They, therefore, conclude that exposure to ionizing radiation within the range of the study (less than 50 to about 100 rads) has a carcinogenic effect on female breast tissue.—*Frederick J. Bonte, M.D.*

FRASER, F. C. Genetic counselling and the physician. *Canad. M. A. J.*, Nov. 16, 1968, *99*, 127–134. (From: The McGill University-Montreal Children's Hospital Research Institute, Montreal, Quebec, Canada.)

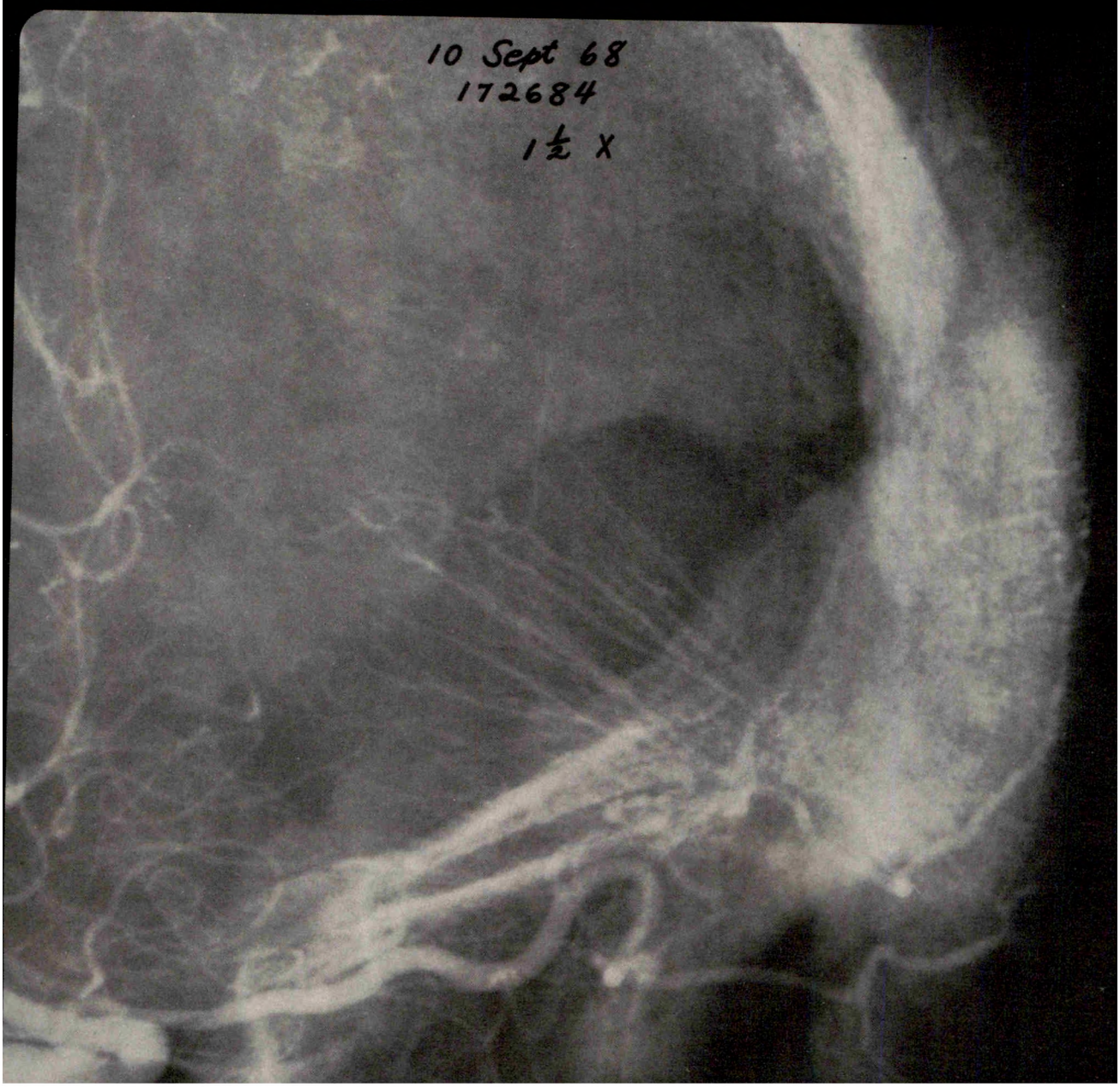
The author discusses the problems of genetic counseling and suggests some specialty training for those who want to do serious work in this area.

In handling a given case, the patient's disease is classified under one of the following categories:

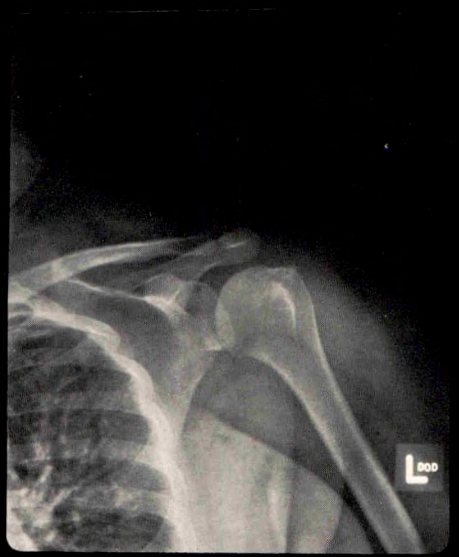
(1) Major mutant genes
(2) Chromosomal aberrations
(3) Combination of genetic and environmental factors, and
(4) Major environmental causes

Examples of some of these categories are given, along with descriptions of counseling approach and patient reaction. The importance of follow-up is emphasized.—*Victor G. Mikity, M.D.*

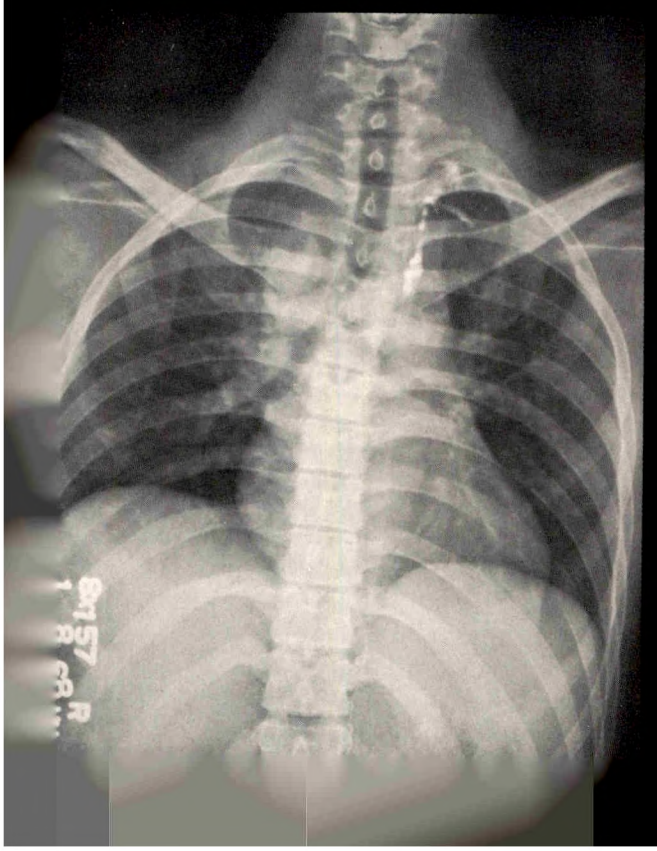
90 second proof



KODAK *RP* X-OMAT Films give more information, time after time



KODAK *RP/L* X-OMAT Medical X-ray film—records the widest possible range of tissue densities.



Quality is the heart of the Kodak 9 Second System. And that's precise why it gives you more information, fil after film, time after tim

In Kodak terms, quality includes fil choice. You actually have a choice o three different Kodak 90-second film You choose which film or films bes meet your requirements re of th information you're after, in your hospita or your private offic

Superior processing is the rest of th Kodak quality story. And it's a shor story: 90 seconds from exposed film t clear readability. The credit goes to th KODAK *RP* X-OMAT Processor workin with the new low-temperature, long-lif processing chemical

The outcome: more information i your radiograph

For quality results in 90 seconds, take the steps you know will lead directly there—with KODAK *RP* X-OMAT products.

Kodak

EASTMAN KODAK COMPAN

Radiography Markets Division, Rochester N

Bright-image fluoroscopy on wheels.

Picker's "Surveyor" lets you wheel the best in fluoroscopy to any needed location. At the bedside, in the emergency or operating room, in the coronary care suite... wherever you find a standard 110 V, 20 amp. outlet... you can have the advantages of modern image-intensified fluoroscopy.

The "Surveyor" has close-coupled, high efficiency optics that yield an excellent picture with minimum radiation.

The "Surveyor" offers the maintenance-free dependability of solid-state TV systems.

The "Surveyor" also permits radiography: built-in cassette holders accommodate either conventional or Polaroid cassettes.

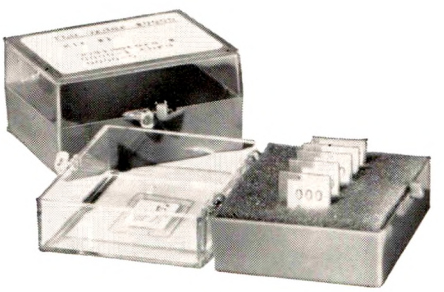
And the Picker "Surveyor" eliminates the frustration of awkward jockeying at the patient's side. This unit can be precisely, rapidly, and simply steered into place by means of its unique power-steered casters. No one else makes maneuvering so easy.

Please contact your local Picker representative for all the details. Or write to the Picker Corporation, 595 Miner Road, Cleveland, Ohio 44143.



PICKER

TLD Custom Dosimeter Service, independently and individually calibrated, now available under professionally controlled standards.



Profit from the unique advantages of this individually calibrated LiF dosimeter for any dosage measurement in which the wide dosage range and large energy independence of these dosimeters offer an advantage. A simple-to-use service for measurement of depth dose, field distribution, and scores of other applications. Offers real exactitude in medical radiation control and testing in diagnostic and therapeutic procedures, or in industrial radiation control and testing. For more complete information on TLD Custom Dosimeter Service in the light of your needs, send full particulars concerning your requirements. No obligation, of course.

Check these advantages of TLD Custom Dosimeter Service against your requirements.

SPECIFICATIONS

Provided in sets of 5 solid state LiF dosimeters plus one control.

- Complete readout and reporting upon return to us.
- Exposure range 10^{-2} to 10^{5}R.
- Each dosimeter individually calibrated.
- Standard error less than 5% for exposures above 100 mr.
- Dose rate independent up to at least 2 x 10^{8}R per second.
- Energy response independent for X and Gamma radiations down to 100 KEV with less than 40% energy dependence for lower energies to 18 KEV.
- Dosimeters can be furnished sealed in sterile tubing.

^{6}LiF, ^{7}LiF, and CaF:Dy solid state dosimeters also available.

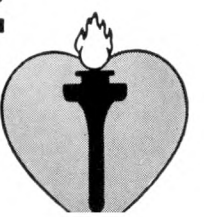
R.S. Landauer JR. & CO.
A Division of Technical Operations, Inc.
Landauer and Gardray Health And Safety Services
GLENWOOD SCIENCE PARK, GLENWOOD, ILLINOIS 60425 (312) 755-7000



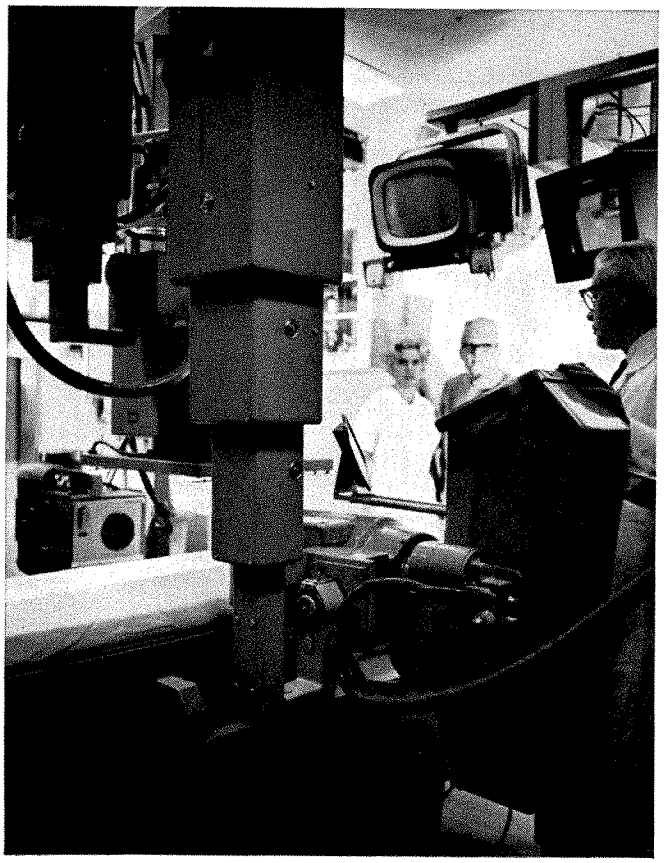
YOU'RE
WHISTLING
IN THE
DARK

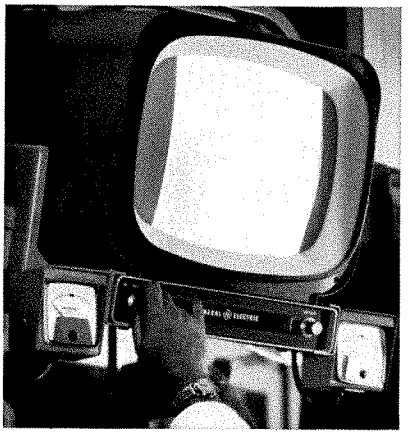
. if you think that heart disease and stroke hit only the other fellow's family.
Fight these killers

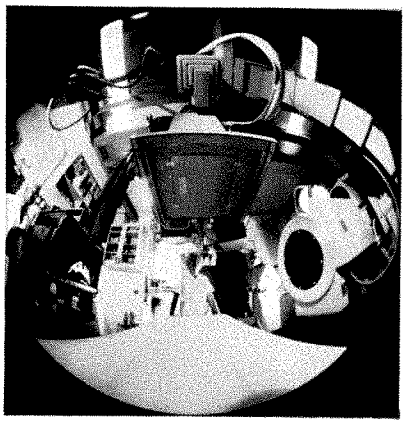
GIVE...
so more will live
HEART
FUND



BI-PLANE SYSTEMS SPECIAL PROCEDURES







Dynamic Diagnosis

Whatever your particular procedure—cerebral, cardiac or abdominal—General Electric special procedures systems are engineered to provide the flexibility to match personal requirements. Alternate or simultaneous recording in two planes of the fluoroscopic or radiographic image delivers a dynamic view. Consistent results are achieved with either cine or rapid film changers. ■ Each General Electric special procedures installation is tailored to meet the range of your particular procedural requirements. Just tell your GE representative what you expect to achieve. He'll provide the system — intensifiers, specialized table, generators, TV, cine, rapid film changers, and other equipment—necessary to deliver the dynamic diagnostic information required.

Progress is our most important product

GENERAL ELECTRIC

X-RAY DEPARTMENT • MILWAUKEE, WIS. 53201

Any minute now, a professional will open that door.





He will be from Ilford

He will be one of our X-ray technical representatives, and within his own specialized field he is as professional as the radiologist himself.

We are particularly proud of our technical representatives. We've tried to make certain that they are carefully trained to be expert in handling the various problems which occur from time to time in every X-ray department. And, we have good reason to believe we have succeeded.

X-ray processing technology is currently undergoing dramatic changes. "Full cycle," "half cycle," and even newer developments have reduced the total processing time of X-ray film from minutes to just seconds.

Chemistry, processors and film have all changed. Ilford technical representatives regard these changes as challenges to their professional know-how and they welcome them. So, next time you have a knotty technical X-ray problem, call in one of our "tech reps". We commend him to you.

He is a professional who can not only assist you with problem-solving but who will be happy to show you how Red Seal on Melinex® will perform in your processing system with Ilfomat chemicals.

ILFORD INC.

West 70 Century Road, P.O. Box 288
Paramus, New Jersey 07652
1217 East El Segundo Boulevard,
El Segundo, California 90245
3566 Elm Street, Hapeville, Georgia 30054

Now!



90 second
Fuji film
type Rx
polyester base

Available through
Pyne X-Ray and
their distributors

PYNE X-RAY CORPORATION
FUJI FILM

U. S. Distributors of FUJI Kx and Rx Film warehoused in New York, Chicago, Los Angeles
Dealers in all cities throughout the country.

The British Journal of Radiology

A monthly publication covering the fields of

DIAGNOSTIC RADIOLOGY, RADIOTHERAPY,
NUCLEAR MEDICINE, RADIATION PHYSICS,
ULTRASONICS, RADIATION PROTECTION,
RADIOBIOLOGY AND RADIATION CHEMISTRY

The British Journal of Radiology, which is the oldest radiological journal in the world (having started in 1896 as *The Archives of Clinical Skiagraphy*) now appears in a new format. The average of 80 pages per month and the number and excellent quality of the illustrations are being maintained and the page size has been increased to 10½ × 7¾ in. to allow wider margins.

An increasing proportion of editorial space is being used to publish original contributions in radiodiagnostic physics and technology, cellular and human radiation biology, the techniques for clinical investigation using labelled compounds and in other rapidly growing fields on the fringe of radiology. A series of review articles on subjects of topical medical and scientific interest has also been inaugurated in addition to the presentation of selected papers which have been read at meetings of The British Institute of Radiology (of which this Journal is the official organ).

Annual subscription: £7.0.0. (U.S. $20.00)

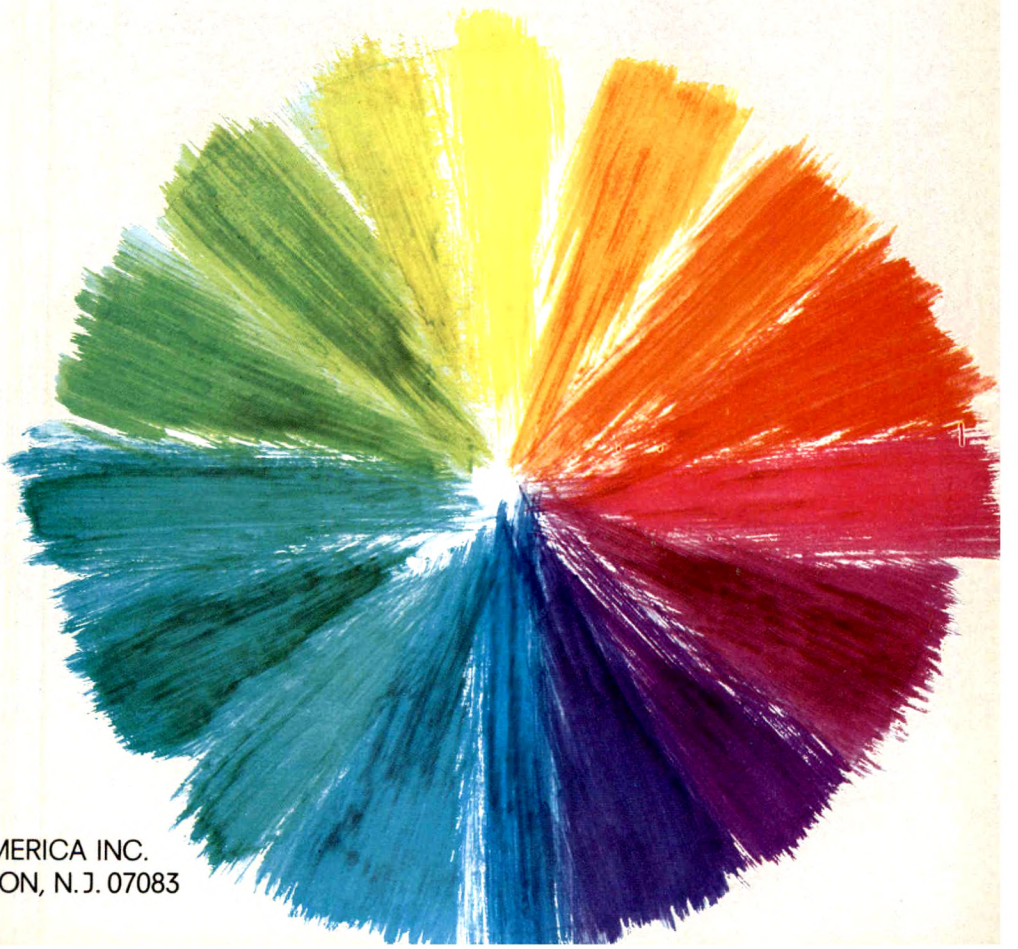
obtainable from

THE BRITISH INSTITUTE OF RADIOLOGY
32 WELBECK STREET, LONDON, W.1
and from leading booksellers all over the world

SIEMENS

From our total commitment

X-ray diagnosis, radiotherapy, nuclear medicine, medical data processing.
We are engaged with the entire spectrum of medical technology.
Our research and development people keep close liaison with medical research and practice, consequently, we are able to offer the physician equipment tailored for his specific tasks.



SIEMENS MEDICAL OF AMERICA INC.
685 LIBERTY AVENUE, UNION, N.J. 07083

SIEMENS

SIREGRAPH System Approach

From its remote control console to the smallest table accessory, the SIREGRAPH is the „System Approach" to the radiologists' most pressing problems – how to obtain the highest possible consistent quality of information and how to make the most efficient use of his time.

Outstanding features include:

- 90/90 continuously variable speed motor driven tilting table
- Rotating cradle (optional)
- Two way power top
- Fully automatic undertable spot film device for use with five various cassette sizes
- Built-in 10/6 SIRECON Image Intensifier with television which tracks the X-ray beam through all angulations of X-ray tube or table
- Routine and special techniques including planigraphy and zonography
- Choice of recording methods from image system 70 mm – 35 mm or 16 mm cine

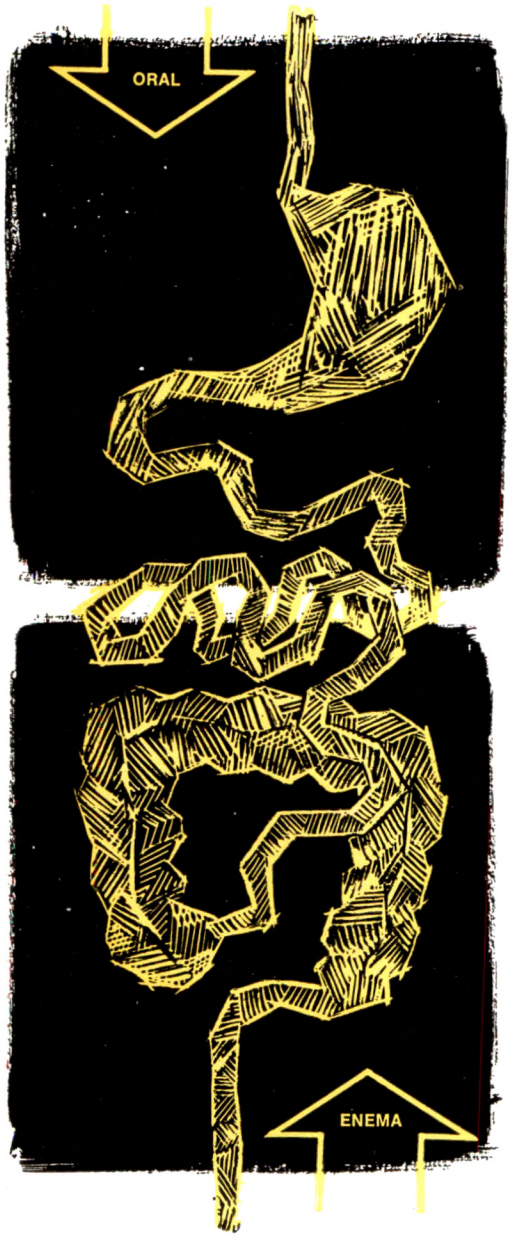
SIEMENS MEDICAL OF AMERICA INC.
685 LIBERTY AVENUE, UNION, N.J. 07083

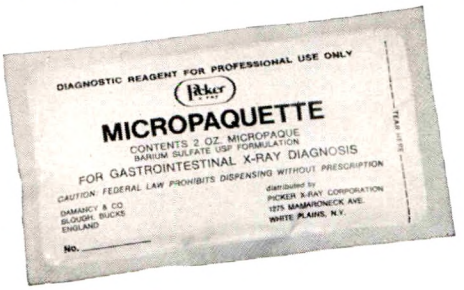


MICROPAQUE now comes premeasured prepackaged for single-use by either route

BARIUM SULFATE U.S.P. FORMULATION

CALCO UNIVERSITY CENTRAL LIBRARY





MICROPAQUETTES are now available with 2 oz. or 4 oz. MICROPAQUE content. Simply empty a packet into your mixer, add indicated water, mix, and there's your correct dose. Content is premeasured by *weight*, not *volume*, so it's easy to whip up the exact quantity you need, with accurate control of density, making it as thick or thin as you want. Convenient, time-saving.



MICROPAQUE DISPOSABLE ENEMA KITS contain everything you need for a single enema: a plastic enema bag, six feet of tubing with a faucet connector on one end, a rectal acorn on the other, and 10 oz. of MICROPAQUE. To use, simply fill the bag with water, knead the bag to mix the charge, and promptly administer. Discard after the examination . . . no measuring, no pouring, no clean-up, no cross-infection hazard.

MICROPAQUE

single-use economy

either way, there's no waste: you mix only as much as you need, one packet or bagful per patient. No unused surplus to squander down the drain. No possibility of contamination with dust or dirt.

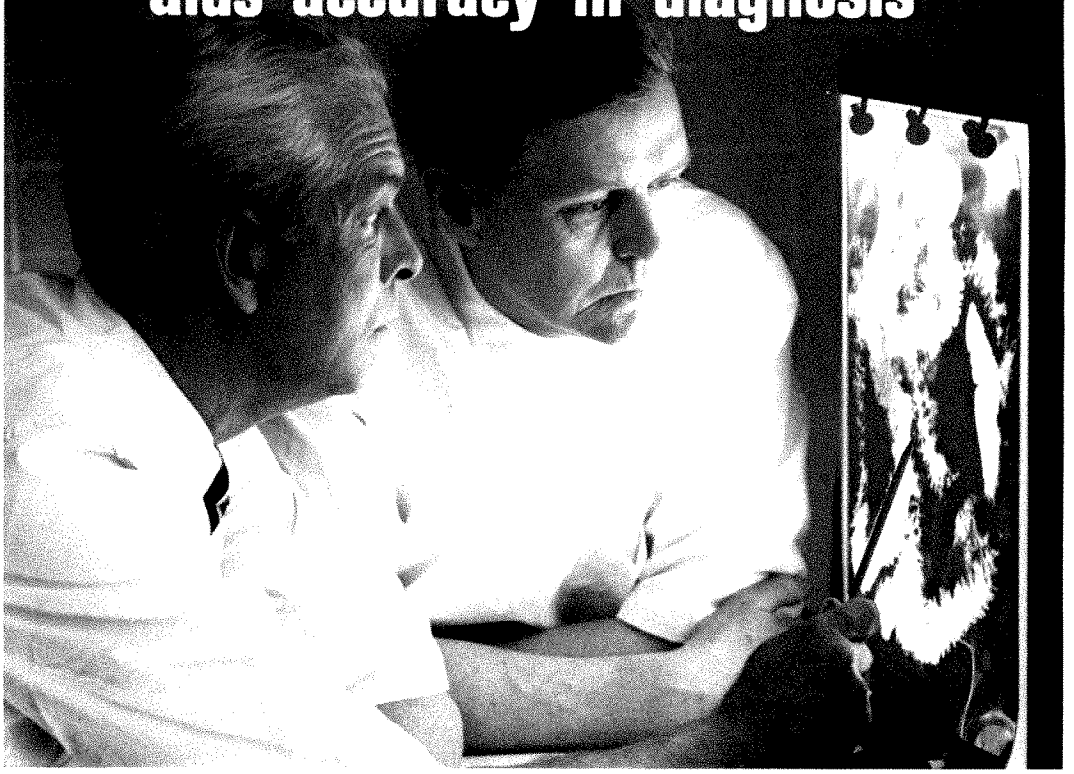
either way, you combine the proven virtues of MICROPAQUE with new ease and accuracy in dispensing.

Ask your local Picker representative
about our special introductory offer on
Micropaquettes and Enema Kits.
Call any local Picker office, or write
Picker X-Ray Corporation, White Plains, New York.

PICKER

BAROLOID

aids accuracy in diagnosis



In G.I.'s, small bowel or air-contrast colon studies, micro-barium BAROLOID aids the radiologist in diagnosis because it spreads evenly, clings to the mucosa, does not break up, crack, peel or flocculate. Provides sharp pictures of slight dilation of bowel loops or abnormal quantities of fluids with standard or high K. V. technics. Rigidly uniform, each batch exactly matches preceding batches. May be prepared as much as a day in advance.

Professional sample available on request.

BELL-CRAIG, INC.

41-14 27th Street L.I.C., N.Y. 11101


complexity


simplicity!
TECHNETOPE II
SQUIBB
CAUTION
RADIOACTIVE MATERIAL

Hiroshima University selects high-energy linac for radiotherapy.



SQUIBB
a research concept in nuclear medicine

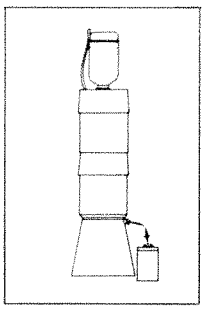
Introducing new Technetope® II

Squibb Technetium 99m STERILE GENERATOR

A FAR SIMPLER GENERATOR . . .
Hooks, hangers, and handles complicate assembly, so you won't find any on Technetope II. It's so simple that, after the usual aseptic techniques, assembly consists basically of two insertions into the generator column. Then attach an eluent bottle, an evacuated collecting vial, and milk. *That's* simplicity.

. . . DESIGNED WITH "T.D.S." IN MIND
Time: Technetope II simplicity reduces assembly time...keeping radiation exposure to a minimum. However, proper radiation safety precautions should be maintained at all times.
Distance: Technetope II allows you to keep your distance. You don't have to be constantly near the generator because it is self-milking. And eluate collection is made *at the side* of the unit—*away* from an unshielded port.
Shielding: Technetope II has another half-value layer of lead shielding—without adding a cumbersome dispenser, additional cost, or special contract.

In addition, Technetope II is readily adaptable to tandem milking which provides high concentrations of ^{99m}Tc per ml.—another Squibb first and exclusive.



Technetope II (Squibb Technetium 99m) Sterile Generator provides a means of obtaining a sterile, non-pyrogenic supply of Technetium 99m (^{99m}Tc). ^{99m}Tc, the short-lived daughter ($T\frac{1}{2} = 6$ hours) of Molybdenum 99 (^{99}Mo, $T\frac{1}{2} = 67$ hours), is obtained from the generator by periodic elution. The amount (in millicuries) of ^{99m}Tc obtained in the initial elution will depend on the original potency of the generator, while the activity obtained from subsequent elutions will depend on the time interval between elutions.

Warning: Proper radiation safety precautions should be maintained at all times. The column containing ^{99}Mo need not be removed from the lead shield at any time. The radiation field surrounding an unshielded column is quite high. Solutions of ^{99m}Tc withdrawn from the generator should always be adequately shielded. The early elutions from the generator are highly radioactive. For radiation protection, a lead shield for the collecting vial is included with Technetope II.

For additional information on this advanced generator or the tandem milking technique, please use the coupon below.

I would like to receive full information on:

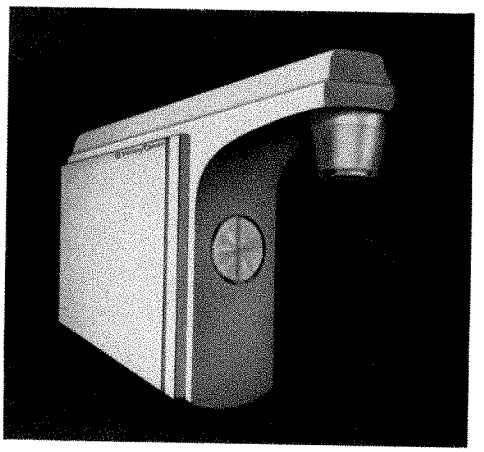
☐ **Technetope® II** (Squibb Technetium 99m) Sterile Generator

☐ Tandem Milking with Technetope II

Please attach this coupon to your letterhead and mail to Medotopes Customer Service Dept., P.O. Box #7, East Brunswick, N. J. 08816.

Medotopes®

Squibb Division of Nuclear Medicine
East Brunswick, New Jersey 08816



Early in 1969, Varian will deliver a new 35-MeV linear accelerator to Hiroshima University. This machine joins the Clinac® 4 and Clinac® 6 in the Varian line of radiotherapy accelerators. It will be used both for the most advanced, sophisticated radiotherapy applications and for very high energy radiation studies.

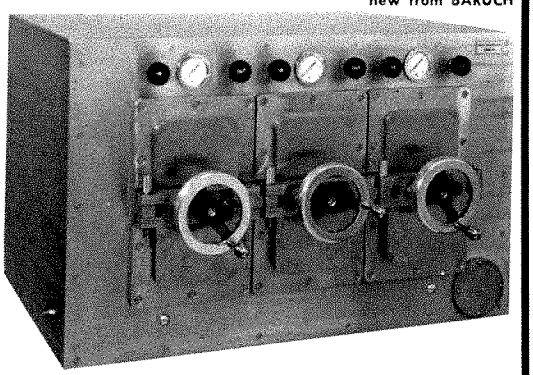
For the radiotherapist, the machine offers: X-ray and electron modes; a wide range of selectable energies and dose rates in either mode; an output easily adjustable from 10 Rmm to over 500 Rmm in both modes; and exceptional field flatness. For the research scientist, a special mode has been included that provides continuous control of electron energy up to 35 MeV and a beam power up to 4.5 kW.

The Hiroshima University linac has a greater X-ray output and occupies less floor space than a betatron, and its installation costs are lower.

If you have a radiotherapy requirement, contact us. We'll be glad to talk about our Clinac capabilities, existing installations, and products. Contact Varian Radiation Division, 611 Hansen Way, Palo Alto, California 94303 or #25 Route 22, Springfield, New Jersey 07081. Varian A. G., Zug, Switzerland.

varian
radiation division

new from BARUCH



radium sterilizing safe

Our maximum capacity Safe is shown above. Effectively shielded to contain up to 1500 mg of radium, this Safe features three individually sealed pressure vessels, each of which can be separately sterilized with ethylene oxide.

We also offer Safes with one pressure vessel shielded for 500 mg of radium and with two pressure vessels shielded for 1000 mg. ALSO AVAILABLE: More lightly shielded versions of the radium safe for **cesium** storage.

VARIED STORAGE ARRANGEMENTS . . .

Select drawer arrangements to meet your storage needs. We offer spacious drawers for molds or applicators, drawers for needles, drawers for capsules. Even drawers for other drawers, enabling rapid transfers to our radium transport cart.

AND INCREASED SAFETY

The controls at the top of the Safe govern the ethylene oxide gas sterilizing system. Now you can have truly sterile radium implants—with increased safety because of reduced handling by your personnel. And handling exposure is also reduced by multi-drawer distribution of sources.

But you can only see the outside here. Get the inside story. Ask us for literature describing our Safe and accessories for radiotherapy —Baruch specializes in solving your radiotherapy equipment problems.

BARUCH INSTRUMENTS CORPORATION
203 North Highland Avenue
Ossining, New York 10562
(914) 762-2255

RECOMMENDED READING FOR ROENTGENOLOGISTS

☐ **X-RAY DIAGNOSIS OF CONGENITAL CARDIAC DISEASE** *by* **Larry P. Elliott** *and* **Gerold L. Schiebler,** *both of Univ. of Florida College of Medicine, Gainesville. Foreword by* **Paul C. Hodges.** '68, 260 pp., 221 il., 3 tables, $11.50

☐ **FUNDAMENTAL PROBLEMS IN SCANNING** *compiled and edited by* **Alexander Gottschalk** *and* **Robert N. Beck,** *both of Univ. of Chicago. (38 Contributors)* '68, 424 pp. (7 × 10), 309 il. (10 in full color), 12 tables, $26.75

☐ **HODGKIN'S DISEASE** *compiled and edited by* **David W. Molander,** *Cornell Univ. Medical College, and* **George T. Pack,** *New York Medical College. Both of New York City. (7 Contributors)* '68, 228 pp. (7 × 10), 121 il., 39 tables, $15.00

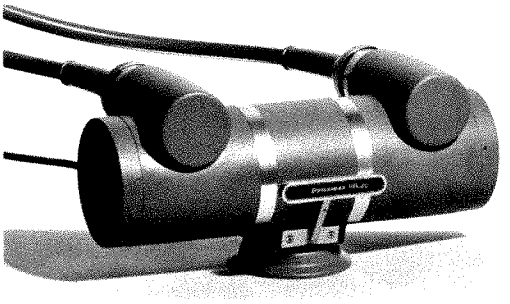
☐ **ROENTGENOLOGY OF THE SPLEEN AND PANCREAS** *by* **Josef Rosch,** *Charles Univ., Prague.* '67, 376 pp. (6¾ × 9¾), 434 il., $29.75

☐ **CANCER THERAPY BY INTEGRATED RADIATION AND OPERATION** *compiled and edited by* **Benjamin F. Rush, Jr.,** *and* **Robert H. Greenlaw.** *Both of Univ. of Kentucky College of Medicine, Lexington. Foreword by* **Charles Tucker.** *(40 Contributors)* '68, 176 pp. (7 × 10), 58 il., 82 tables, $12.75

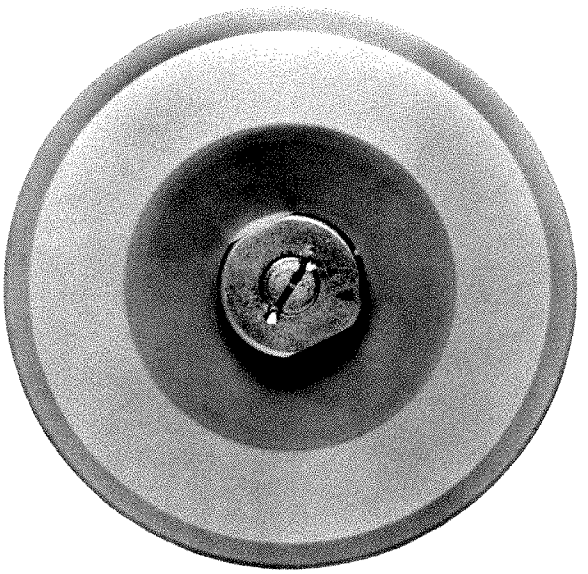
☐ **INTRAVENOUS ABDOMINAL AORTOGRAPHY AND PLACENTOGRAPHY** *by* **Melvin H. Schreiber, Fred J. Wolma,** *and* **Charles K. Hendrick.** *All of Univ. of Texas Medical Branch, Galveston.* '67, 68 pp. (7 × 10), 66 il. (3 in color), $8.75

☐ **CERVICAL SPONDYLOSIS AND ITS NEUROLOGICAL COMPLICATIONS** *by* **Bernard H. Smith,** *State Univ. of New York at Buffalo.* '68, 240 pp. (6¾ × 9¾), 101 il., $12.00

CHARLES C THOMAS • PUBLISHER
301-327 East Lawrence Avenue
Springfield · Illinois · 62703



To extend the range of performance: The Dynamax "HD50"

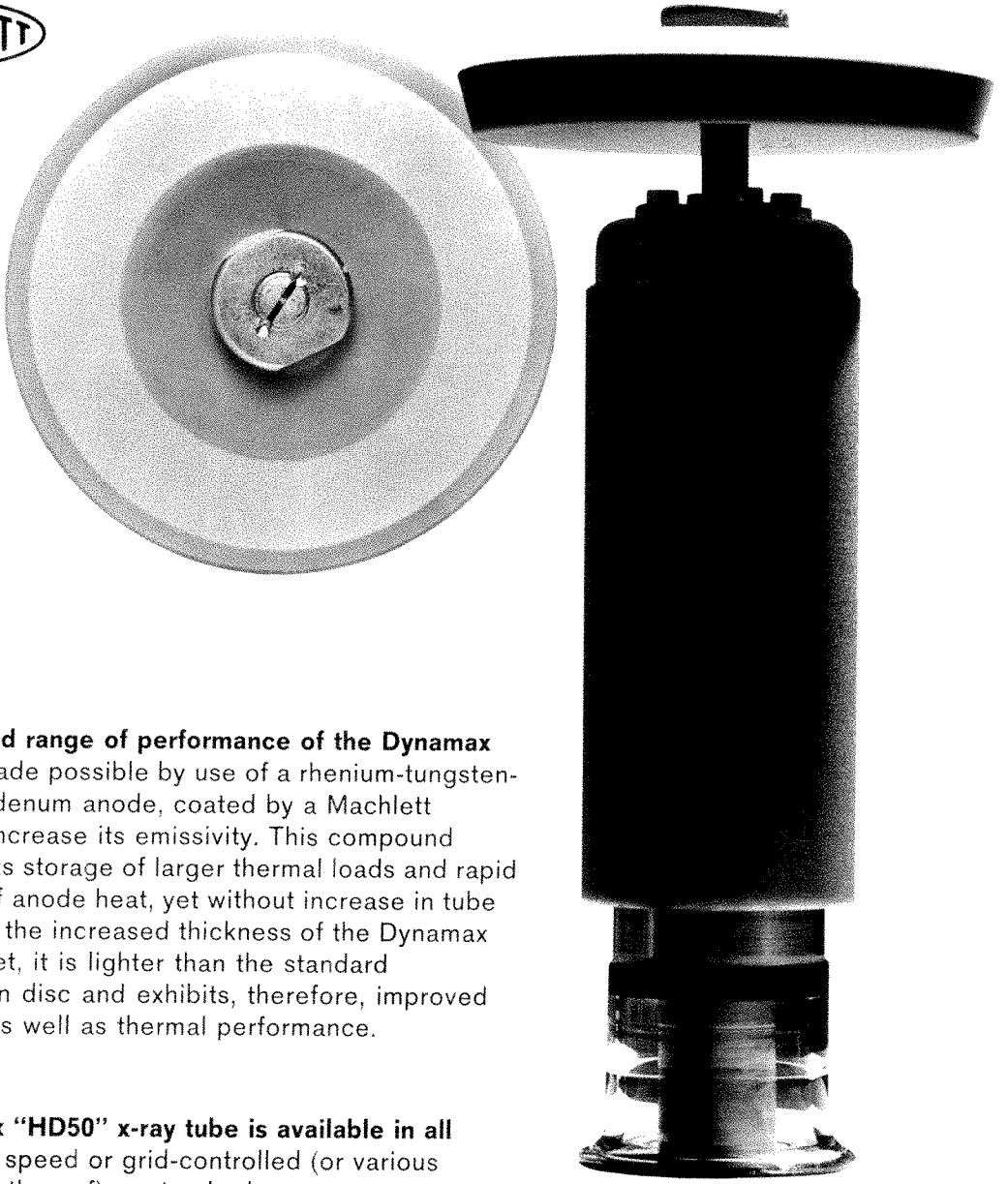


The Dynamax "HD50" now employs a rhenium tungsten-faced molybdenum anode.

With this new compound 175,000 HU anode in the Dynamax "HD50", cine-radiographic and angiographic film run times can be extended, and routine work loads significantly increased.

MACHLETT

MACHLETT

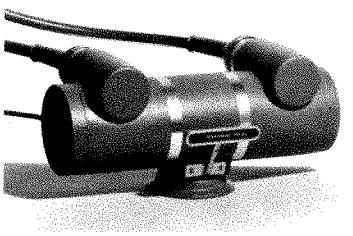


The increased range of performance of the Dynamax "HD50" is made possible by use of a rhenium-tungsten-faced molybdenum anode, coated by a Machlett process, to increase its emissivity. This compound anode permits storage of larger thermal loads and rapid dissipation of anode heat, yet without increase in tube size. Despite the increased thickness of the Dynamax "HD50" target, it is lighter than the standard solid tungsten disc and exhibits, therefore, improved mechanical as well as thermal performance.

The Dynamax "HD50" x-ray tube is available in all options: high speed or grid-controlled (or various combinations thereof) or standard.

Important Note: The Dynamax "HD50" insert may be used in all standard Dynamax housings, including the Dynamax "HD25", "HD26"; Dynamax "40", "46", "OR40"; and the Dynamax "50". The "HD50" insert may be obtained either as a replacement or when ordering a new tube.

For details on the Dynamax "HD50" rotating anode x-ray tube, write: The Machlett Laboratories, Inc., Springdale, Connecticut 06879.

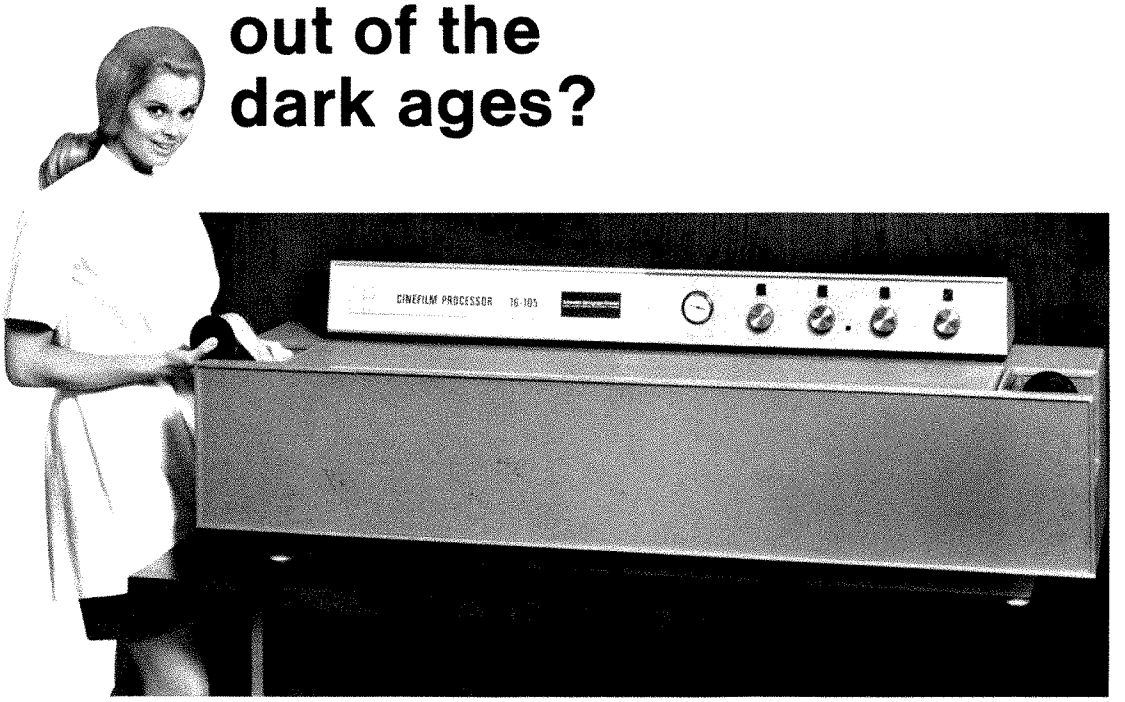


RAYTHEON

THE MACHLETT LABORATORIES, INC.

A SUBSIDIARY OF RAYTHEON COMPANY

Who took film processing out of the dark ages?



We did.

With the first really flexible film processor that works in daylight as well as dark.

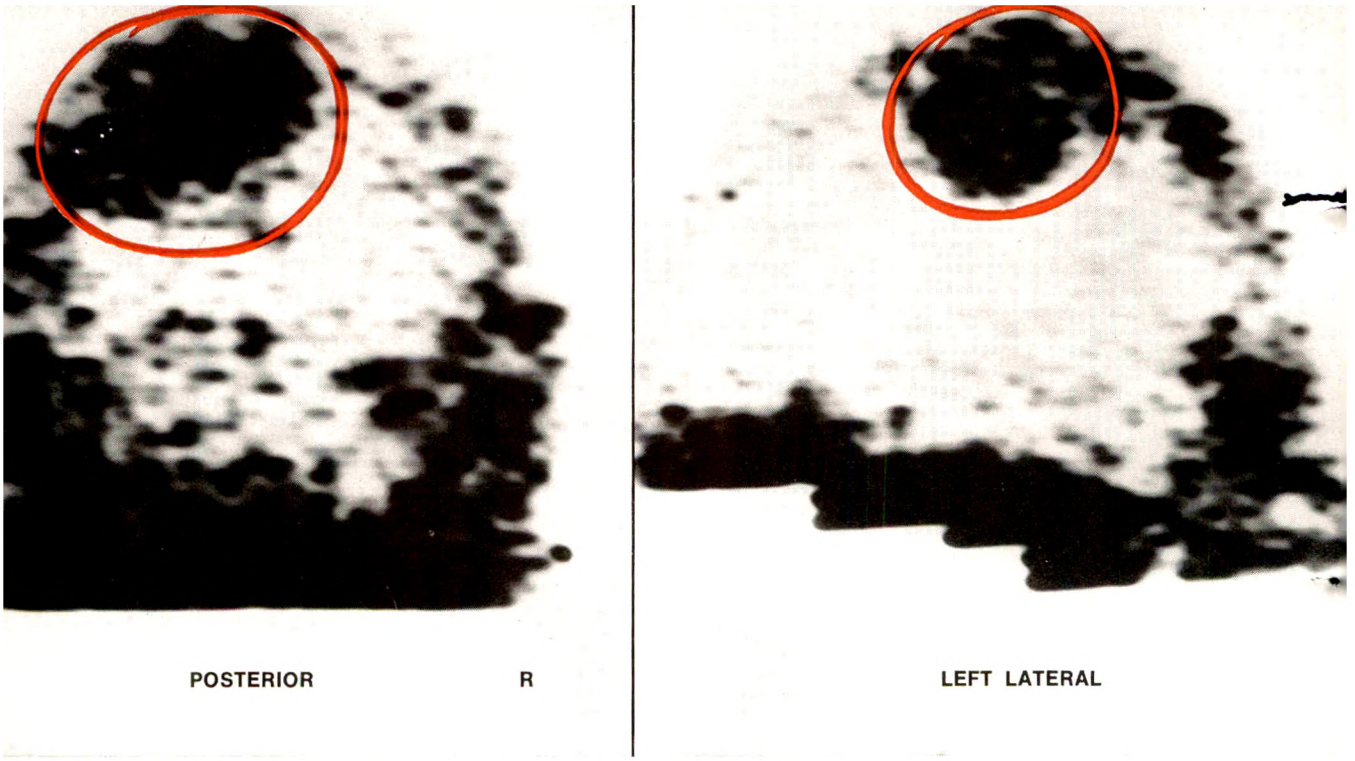
It's self threading. Needs no leader with most films. You can feed it any size film—from 16 mm to 105 mm (a full 5 inches wide). In pieces as short as 5 inches long. At random. Interchangeably.

And that's not all. New, ingenious cassette design makes loading a cinch. Built-in controls deliver consistent results, no matter who the operator. And a simple water flush is absolutely the only daily maintenance the unit needs.

We'll be glad to show you how this award-winning, table-top processor fits into any nook, freeing some of your darkroom space for more productive use. Phone your local x-ray dealer or write direct.

Let us bring a little light into your life.

Automatic Seriograph Division
Litton Medical Products Group, Litton Industries
515 East Touhy Avenue • Des Plaines, Illinois 60018 • Telephone: (312) 296-4488



POSTERIOR R

LEFT LATERAL

In suspected brain pathology, find out fast with **Pertscan**-99m

For brain scanning, Pertscan-99m provides more information with less radiation to the patient than any other related cerebral test—whether other radioisotopes or x-rays. And you get each projection fast—as little as 2 minutes with a camera, 15 minutes or less with rectilinear scanners.

A 54-year-old man was hospitalized with progressive weakness of the right side, followed by seizures of the right side (Jacksonian seizures). Brain scans showed an abnormal concentration of isotope in the left parasagittal area. Surgery revealed a meningioma, which was removed, and the patient recovered.

The 2 scans above, showing the marked abnormal uptake (which turned out to be a menigioma), were made with Pertscan-99m. This product is shipped Monday through Friday—and Sunday. Thus, brain scans can be scheduled 6 days a week—Monday through Saturday.

INDICATIONS: Adjunctive diagnostic aid in detecting and localizing intracranial neoplastic (primary or metastatic) and non-neoplastic lesions.

CONTRAINDICATIONS: Radio-pharmaceutical agents should not be administered to pregnant women or to persons less than 18 years old unless the indications are very exceptional.

PRECAUTIONS: Care should be taken to ensure minimum radiation exposure to the patient as well as all personnel; to prevent extracranial contamination because this can lead to erroneous interpretation; and to differentiate areas of abnormal activity from areas of normal vascular activity.

Pertscan™-99m
SODIUM PERTECHNETATE Tc 99m

Also available:

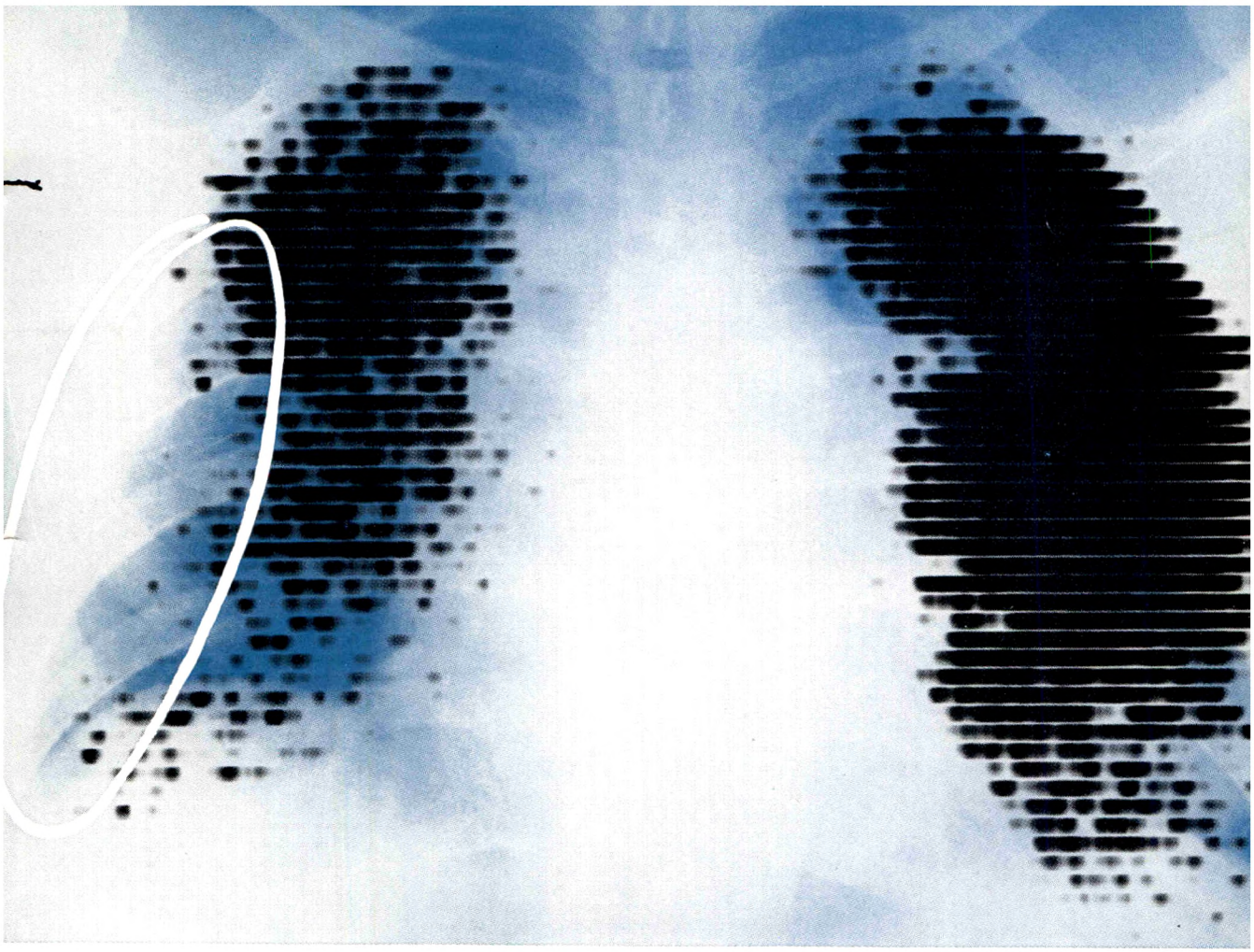
Pertgen™-99m
TECHNETIUM 99m GENERATOR KIT

ABBOTT LABORATORIES NORTH CHICAGO, ILLINOIS

Abbott Laboratories, S.A., 2, rue Thalberg, 1201 Geneva, Switzerland

TM—Trademark

901102



If it's a pulmonary problem, **Macroscan-131** pictures it!

A 50-year-old man was hospitalized after complaining of vague chest pains. Shortly after, he suffered a cardiac arrest. An EKG showed no evidence of cardiac infarction. A lung scan revealed a decreased concentration of isotope in the right lower lobe. This was diagnosed as a pulmonary infarct, therapy was instituted, and the patient recovered.

His scan above, showing the marked diminished uptake, was made with Macroscan-131. This product has many diagnostic uses:

Pulmonary embolism, suspected: To confirm (or rule out) its occurrence.

Chronic pulmonary tuberculosis: To estimate unilateral and regional function and perfusion of the lungs.

Emphysema: To evaluate the decreased regional blood flow that occurs with obstruction of vessels.

Pneumonitis: To evaluate the decreased regional blood flow that occurs without obstruction of vessels.

Lung Tumors: To evaluate the regional ischemia resulting from compression or obstruction of pulmonary arteries.

Surgery and/or other therapy for lung disorders: To evaluate the effectiveness of therapeutic measures.

Macroscan-131 is sterile and non-pyrogenic. It is ready to use and should not be heated prior to use.

INDICATIONS: For scintillation scanning of the lungs to evaluate total, unilateral, and regional arterial perfusion of the lungs.

CONTRAINDICATIONS: Radio-pharmaceutical agents should not be administered to pregnant women or to persons less than 18 years old unless the indications are very exceptional.

PRECAUTIONS, SIDE EFFECTS: Care should be taken to administer the minimum dose consistent with safety and validity of data. The possibility of an immunological response to albumin should be kept in mind when serial scans are performed. There is a theoretical hazard in acute cor pulmonale, because of the temporary small additional mechanical impediment to pulmonary blood flow. A possible case of urticaria has been related to a similar preparation. The thyroid gland should be protected by prophylactic administration of concentrated iodide solution.

Macroscan™-131

AGGREGATED RADIO-IODINATED (I^{131}) ALBUMIN (HUMAN)

ABBOTT LABORATORIES NORTH CHICAGO, ILLINOIS

TM—Trademark.

Abbott Laboratories, S.A., 2, rue Thalberg, 1201 Geneva, Switzerland

When not seeing is believing

The full, precise visualization of the gallbladder obtained with TELEPAQUE is diagnostically important because it assures you that there is no cholecystic pathology. The fact that TELEPAQUE produces a complete picture proves the gallbladder is functioning normally.
But more important is the fact that TELEPAQUE, unlike other contrast agents, does *not* passively fill a diseased gallbladder. Thus the absence of visualization can be of great significance suggesting disease. With TELEPAQUE it is possible to detect those patients with cholecystitis who do not have stones. This indication of pathology, that TELEPAQUE provides adds to its reliability for diagnosis.

Use of TELEPAQUE in a series of 1,207 cholecystographic examinations resulted in 98.3% diagnostic accuracy.* TELEPAQUE has been used in more than 33,000,000 patients... an unparalleled record of tolerance.

Contraindications: Contraindicated in advanced hepatorenal disease or severe impairment of renal function, severe gastrointestinal disorders that prevent absorption, and in patients sensitive to iodine compounds.

Precautions: Severe, advanced liver disease may interfere with metabolism of Telepaque, thus increasing the excretory load on the kidneys. Although renal difficulty has rarely been attributed to Telepaque, renal function should be assessed before cholecystography in severe, advanced liver disease, and renal output and hepatic function should be observed for a few days after the procedure. Patients with preexisting renal disease should not receive high doses of cholecystographic media. Possible renal irritation in susceptible individuals could result in reflex vascular spasm with partial or complete renal shutdown. Caution is advised in patients with coronary disorders, especially those with recent symptoms of coronary artery disease. Blood pressure should be observed after administration of cholecystographic media to these patients. Elevation of protein-bound iodine for several months and false positive urine albumin tests (for three days) may occur after ingestion of iodine-containing cholecystographic media.

Adverse Reactions: Most reactions are mild and transitory; serious side effects are very rare. Gastrointestinal effects (diarrhea, cramps, nausea, vomiting) are the most common. Usually the diarrhea consists merely of a few loose stools, although in isolated cases it may be severe. A mild stinging sensation during urination may occur, and rarely, skin rash, urticaria, pruritus, and flushing. One case of thrombocytopenia has been reported in a patient with a history of conjunctival hemorrhages. Subjective complaints have been: dryness of throat, burning on swallowing, heartburn, sore throat, dizziness, and headache.

Usual Dosage: 3 Gm. (6 tablets) at night after a light supper.

Supplied: Tablets of 500 mg., envelopes of 6 tablets, boxes of 5 and 25 envelopes; also bottles of 500.

*Baker, H. L., Jr., and Hodgson, J. R. (Mayo Clinic and Mayo Foundation): Further studies on the accuracy of oral cholecystography, *Radiology 74*:239, Feb., 1960.

Telepaque® **in oral cholecystography and cholangiography provides the accurate picture with excellent tolerance**

brand of **iopanoic acid**

Winthrop **PIONEERS IN PRODUCTS FOR RADIOLOGIC DIAGNOSIS**

WINTHROP LABORATORIES
NEW YORK, N.Y. 10016

INDEX TO ADVERTISERS

Abbott Laboratories ..... xvi, xvii, lxxviii, lxxix
Amersham/Searle Corporation ..... xxv, xxvii
Atomic Energy of Canada Ltd. xli
Automatic Seriograph Corporation, The (Div. of Litton Industries) lxxvii

Baird-Atomic, Inc. lxxxiv
Barnes-Hind Barium Products ..... xxxviii, xxxix
Baruch Instruments Corporation lxxiv
Becton, Dickinson and Company ..... x, xi
Bell-Craig, Inc. lxviii
Brayten Pharmaceutical Co. vii

Eastman Kodak Company ..... lv, lvi, lvii
Elema-Schonander, Inc. xliv

Fleet Co., C. B., Inc. xxi

General Electric Company ..... xxxiii, xxxiv, xxxv, xxxvi, lxi

Hanley Medical Equipment Company xl
Halsey X-Ray Products Company xxvi
Hida Electric Apparatus Industrial Co., Ltd. xl
High Voltage Engineering i

Ilford, Inc. lxii
Isotopes vi

Keleket X-Ray Corporation viii

Landauer, R. S., Jr. & Company lix
Liebel-Flarsheim Company (Div. of Ritter-Pfaudler Corporation) xxix

Machlett Laboratories, Inc. ..... lxxv, lxxvi
McElroy, Donald, Inc. xxviii

Nicholas Laboratories, Ltd. lxvii
Nuclear Associates, Inc. xxviii
Nuclear-Chicago Corporation ..... xviii, xix

Ohio-Nuclear, Inc. xii

Picker Nuclear Corporation ..... Second Cover
Picker X-Ray Corporation ..... lviii, lxxxiii, Fourth Cover
Profexray, Inc. ..... xxii, xxiii
Purdue Frederick Company, The v
Pyne X-Ray Corporation lxiii

Schick X-Ray Company xx
Schneeman Electronics, Inc. xl
Shintron, Inc. xxxvii
Siemens Medical of America, Inc. ..... lxv, lxvi
Squibb, E. R., & Sons, Inc. ..... xiii, xiv, xv, lxix, lxx, lxxi

Thomas, Charles C, Publisher ..... xxiv, lxxiv

United States Radium Corporation ix

Varian Radiation Division ..... lxxii, lxxiii

Westinghouse X-Ray Division ..... xlii, xliii
Winthrop Laboratories ..... xxx, xxxi, xxxii, xlv, xlvi, xlvii, xlviii, xlix, l, li, lii, liii, liv, lxxx, lxxxi
Wolf X-Ray Corporation ..... Third Cover

We try to present an accurate index. Occasionally this may not be possible because of a last-minute change or an omission.



Ask him to prove it.

(When your Picker man says X-Nog™ is the best tasting high-fat meal around, please ask him to prove it.)

X-Nog is a remarkably palatable, ready-to-use, high fat beverage for x-ray procedures. Exceptional taste (like a first-rate egg nog), pleasant aroma. No unpleasant aftertaste.

X-Nog is sterilized and needs no refrigeration until opened. Easy to use: shake, open, pour. No mixing. No fuss.

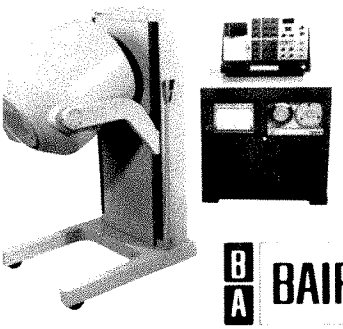
X-Nog, developed by Borden, Inc., sold by Picker, is also economical.

So now when your Picker man brags about the taste of X-Nog, please ask him to prove it. Or write Picker Corporation, 1275 Mamaroneck Avenue, White Plains, New York 10605.

PICKER

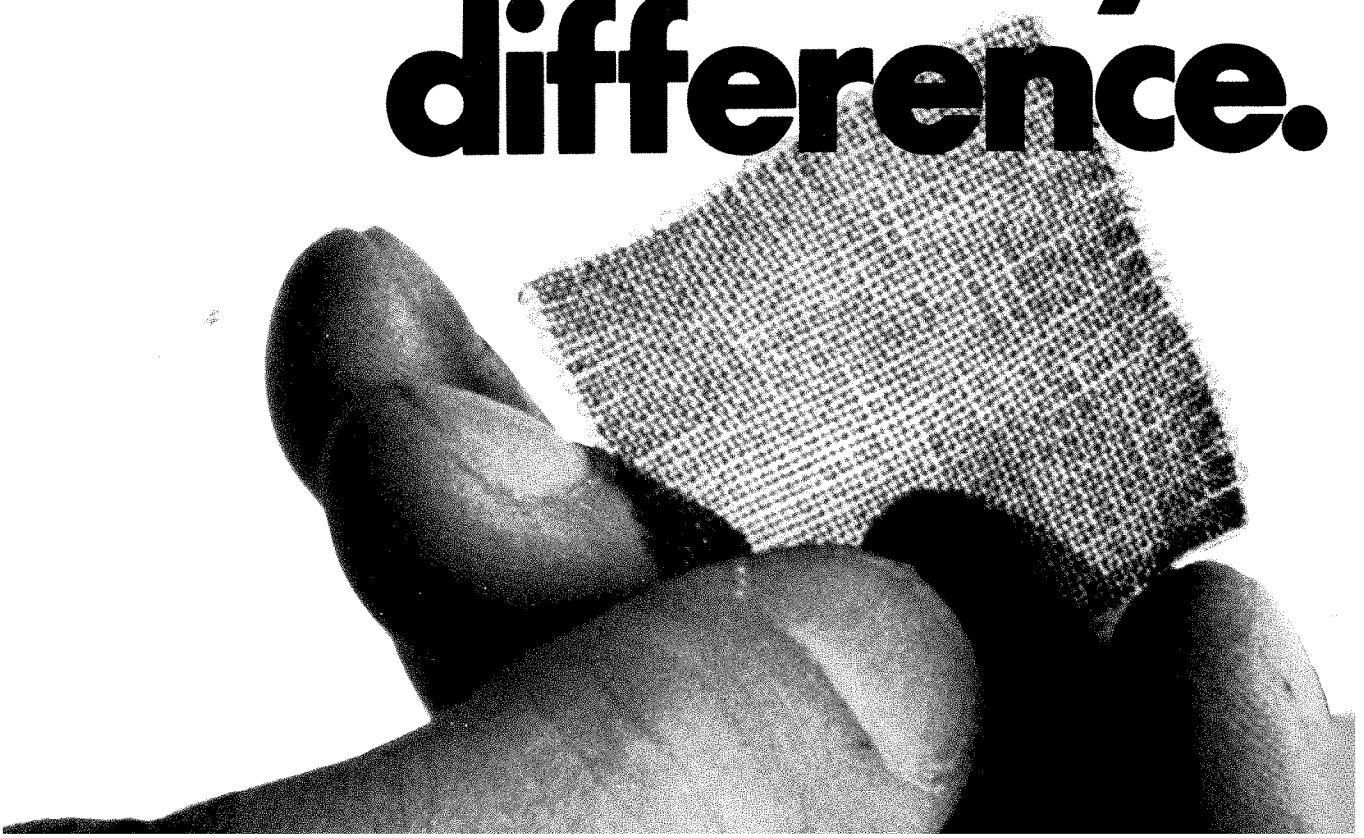
Inlike other scintillation cameras, Baird-Atomic's Autofluoroscope eatures computer-type memory. And that's saying a lot.

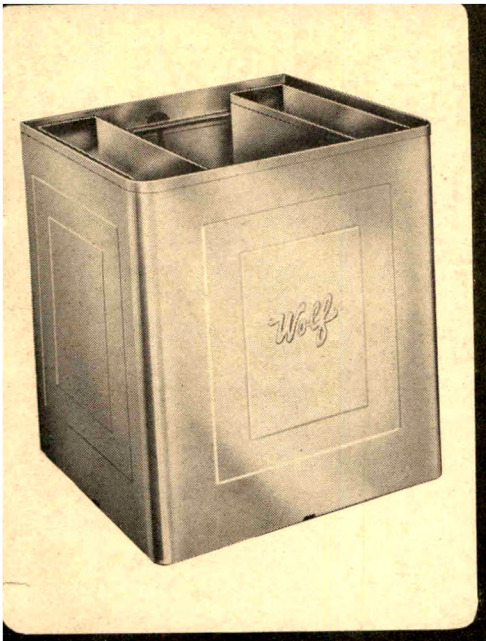
says our non-volatile magnetic core memory can store raw digital data for each picture element. And *restore* age plane uniformity. It lets you flag any areas of the picture for numerical integration in dynamic studies. It rmits fast storage on magnetic tape to provide more data points in dynamic studies. It lets you play back patient data in its original form at any time. Instantly. And because of magnetic core memory, the picture has the same integrity as the raw data. The fact is, magnetic core storage makes the Autofluoroscope a fundamentally more practical and objective tool. What's more, it's faster and easier to use in all procedures than other cameras. So if you're going to buy or lease an imaging device, you should talk to Baird-Atomic before you make your final decision. You owe it to yourself to fully understand why the tiny difference will make such a big difference to your program. Naturally, if you're not already thinking about the Autofluoroscope, we may not change your mind. But we'll give you a tough decision to make. Call for an appointment. 33 University Road, Cambridge, Massachusetts 02138. Telephone: 617 864-7420. Baird-Atomic urope, The Hague, The Netherlands. Baird-Atomic Limited, Hornchurch, England.



BA BAIRD-ATOMIC

The tiny difference.







BRILLIANT DEVELOPMENT

The doctor's diagnosis and the well-being of his patient often depend upon the development of clear, sharp X-rays. There margin for error, no room for second best... and so it must be way with the equipment you use. Herein lies the importance of usin advanced, all-new WOLF Stainless Steel Developing Tank with remov inserts... precision engineered to be the finest of its kind in the world signed to be the reliable workhorse today's advanced science of r genology demands! When you're ready to order, just remember tha greatest x-ray technician, using the finest machine and film available, await, rely and act upon the results produced in his developing tank. "WOLF" has proven to be the name you can rely on, everytime!

For your free brochure with complete details, write your dealer or Wolf today.

WOLF X-RAY CORPORATION

NEW YORK • CHICAGO • LOS ANGELES • TORONTO

Executive Offices: 182-20 Liberty Avenue, Jamaica, New York 11412

WOLF X-RAY CORP. Wolf NEW YORK

Somewhere near you, a radiologist is getting the sharpest images he's ever seen because of this new table.

Hundreds of radiologists now working with the new Picker "Galaxy" table are getting the best images they've ever experienced: the sharpest fluoroscopy, spotfilms, and Bucky radiographs. And because their everyday practical experience is likely to be more revealing than our technical explanations, you might wish to seek out a current user of the "Galaxy" table. (If you need help with this search, let us know. We'll help you set up a visit.)

Until then, the following technical explanations can provide background as to why the "Galaxy" table produces such superb images.

The table is so structurally rigid that it thoroughly tames the subtle (and some not-so-subtle) vibrations all too often encountered in x-ray tables. The improvement in image sharpness resulting from such suppression is dramatic.

The "Galaxy" collimating system optimizes imaging geometry by significantly refining the relationship of focal spot, shutter plane, film plane, and patient plane. Geometric unsharpness and penumbra, for instance, are abated by locating the fluoroscopic shutter 30% farther from the focal spot than is customary.

Another important point about the "Galaxy" system is the way its automatic coning improves radiographic contrast, reduces scatter radiation, and minimizes dosage to patients and operators.

And now for help in finding a nearby "Galaxy" table user to speak to—or for more information from us—contact your local Picker representative or write Picker Corporation, 595 Miner Road, Cleveland, Ohio 44143.

PICKER



CALCUTTA UNIVERSITY CENTRAL LIBRARY
19 JUL 1969

FOUNDED IN 1906 AS THE AMERICAN QUARTERLY OF ROENTGENOLOGY

THE AMERICAN JOURNAL OF ROENTGENOLOGY RADIUM THERAPY AND NUCLEAR MEDICINE

OFFICIAL ORGAN OF

THE AMERICAN ROENTGEN RAY SOCIETY
THE AMERICAN RADIUM SOCIETY

TRAIAN LEUCUTIA, Editor
KENNETH L. KRABBENHOFT, Assistant to the Editor

ASSOCIATE EDITORS

HARRY HAUSER RUSSELL H. MORGAN EDWARD B. D. NEUHAUSER

CONSULTING EDITORIAL BOARD

OSCAR V. BATSON
JOHN CAFFEY
ROSS GOLDEN
PAUL C. HODGES
HOWARD B. HUNT
JOHN H. LAWRENCE
REED M. NESBIT
EUGENE P. PENDERGRASS
LAURISTON S. TAYLOR
OWEN H. WANGENSTEEN
SHIELDS WARREN

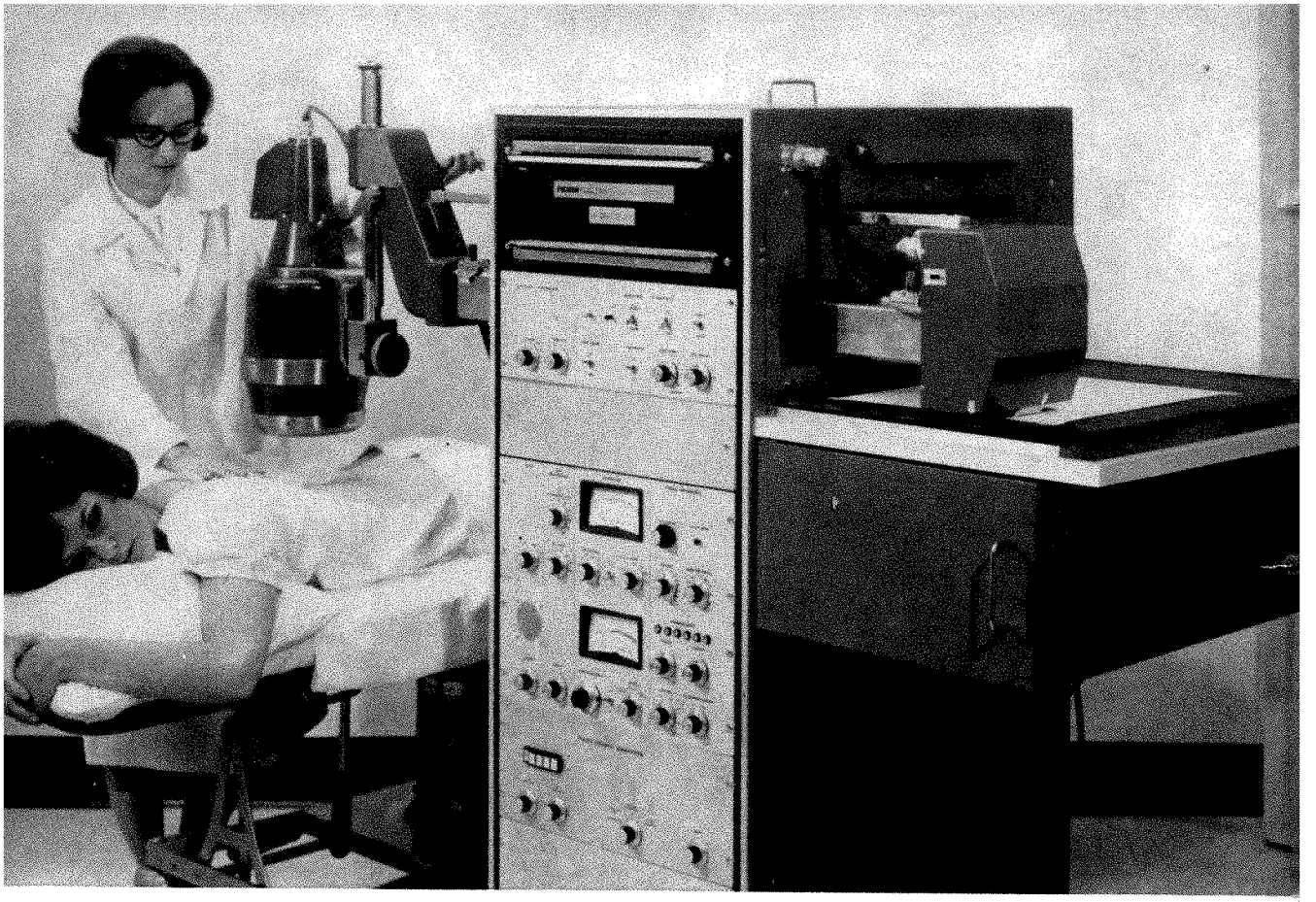
Issued Monthly for the American Roentgen Ray Society by

CHARLES C THOMAS · PUBLISHER · SPRINGFIELD · ILLINOIS · 62703

VOLUME 105 MARCH, 1969 NUMBER 3

Fifty-first Annual Meeting, American Radium Society
Bellevue Stratford Hotel, Philadelphia, Pennsylvania 19102
April 27-30, 1969

For Preliminary Program see January Issue



The case for the classical radioisotope scanner, or...

Why does Picker keep refining and improving its basic rectilinear scanner (Magnascanner® 500), when it also has a most sophisticated high-speed scanner (Dynapix®), and two exceptional cameras (Dynacamera™ and Magnacamera®)?

Because: despite the rapid forward thrust of progress —which we ourselves aid, abet, foster and contribute to —nothing we or anyone else has done has obsoleted the basic rectilinear scanner. What basic scanners do, nothing does better, and few do as well. Examples?

For a small hospital starting a diagnostic radioisotope laboratory with a small patient load and a modest budget, there is nothing quite as appropriate as a scanner. Hence, four out of five nuclear medicine departments get started with a Magnascanner and there are now over 2500 in use throughout the world. Similarily, a Magnascanner is a most relevant choice for larger hospitals in need of an instrument with the highest resolution for diagnostic confirmation. A basic scanner like the Magnascanner is still the best device available for static-imaging applications by virtue of its very high resolution, large field of view, wide energy range, contrast enhancement, wide choice of focusing collimators, and modest cost.

None of this should imply that the Magnascanner is an untouched island in the stream of progress. Today's instrument is generations away from yesterday's. Note: (1) maximum scan speed has been increased from 200 cm/min to 500 cm/min; (2) detector can be positioned by a control on the detector head itself, and a ratemeter on the detector head facilitates and speeds location of "hot" and "cold" spots; (3) a new color photo recording system is available in addition to black and white photorecording, multicolor dot recording, and Teledeltos black dot recording; (4) push button energy window selection (in addition to manual selection) for the most common radioisotopes used in diagnosis.

And Now the Dual Magnascanner®—This instrument is essentially identical to the Magnascanner® 500 except that it has two separate opposed detectors which acquire information independently. AP and PA, or RL and LL rectilinear scans can be performed simultaneously. This capability minimizes the need for patient re-positioning and reduces the scanning time by half.

Further information is available—Please write for detailed information on the Magnascanner® 500 and the Dual Magnascanner to Picker Nuclear, 1275 Mamaroneck Avenue, White Plains, N.Y. 10605. Please request file 235R.

PICKER

FOUNDED IN 1906 AS THE AMERICAN QUARTERLY OF ROENTGENOLOGY

THE AMERICAN JOURNAL OF ROENTGENOLOGY RADIUM THERAPY AND NUCLEAR MEDICINE

OFFICIAL ORGAN OF

THE AMERICAN ROENTGEN RAY SOCIETY

THE AMERICAN RADIUM SOCIETY

TRAIAN LEUCUTIA, Editor

KENNETH L. KRABBENHOFT, Assistant to the Editor

ASSOCIATE EDITORS

HARRY HAUSER RUSSELL H. MORGAN EDWARD B. D. NEUHAUSER

CONSULTING EDITORIAL BOARD

OSCAR V. BATSON
JOHN CAFFEY
ROSS GOLDEN
PAUL C. HODGES
HOWARD B. HUNT
JOHN H. LAWRENCE
REED M. NESBIT
EUGENE P. PENDERGRASS
LAURISTON S. TAYLOR
OWEN H. WANGENSTEEN
SHIELDS WARREN

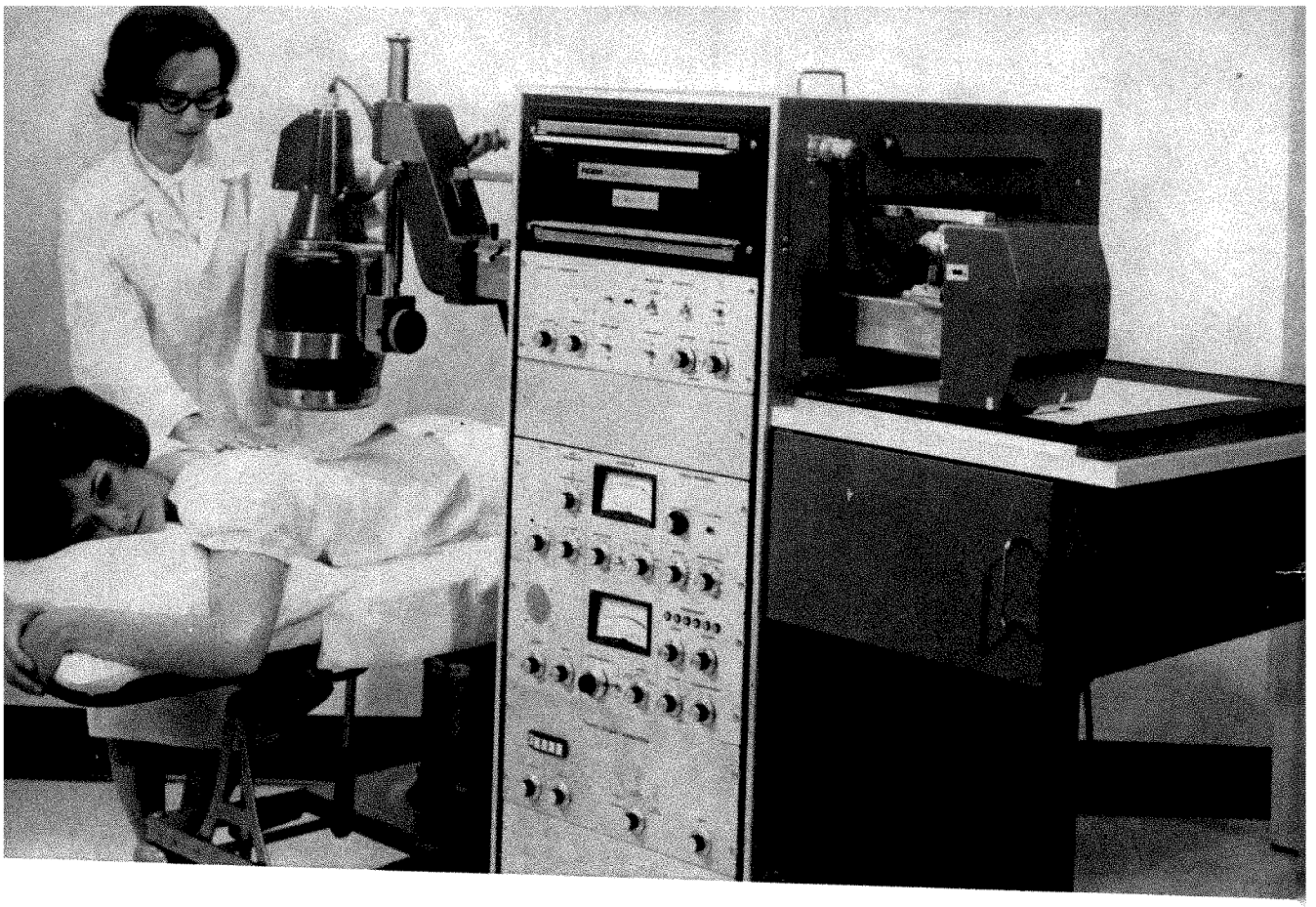
Issued Monthly for the American Roentgen Ray Society by

CHARLES C THOMAS · PUBLISHER · SPRINGFIELD · ILLINOIS · 62703

VOLUME 105 MARCH, 1969 NUMBER 3

Fifty-first Annual Meeting, American Radium Society
Bellevue Stratford Hotel, Philadelphia, Pennsylvania 19102
April 27-30, 1969

For Preliminary Program see January Issue



The case for the classical radioisotope scanner, or...

Why does Picker keep refining and improving its basic rectilinear scanner (Magnascanner® 500), when it also has a most sophisticated high-speed scanner (Dynapix®), and two exceptional cameras (Dynacamera™ and Magnacamera®)?

Because: despite the rapid forward thrust of progress —which we ourselves aid, abet, foster and contribute to —nothing we or anyone else has done has obsoleted the basic rectilinear scanner. What basic scanners do, nothing does better, and few do as well. Examples?

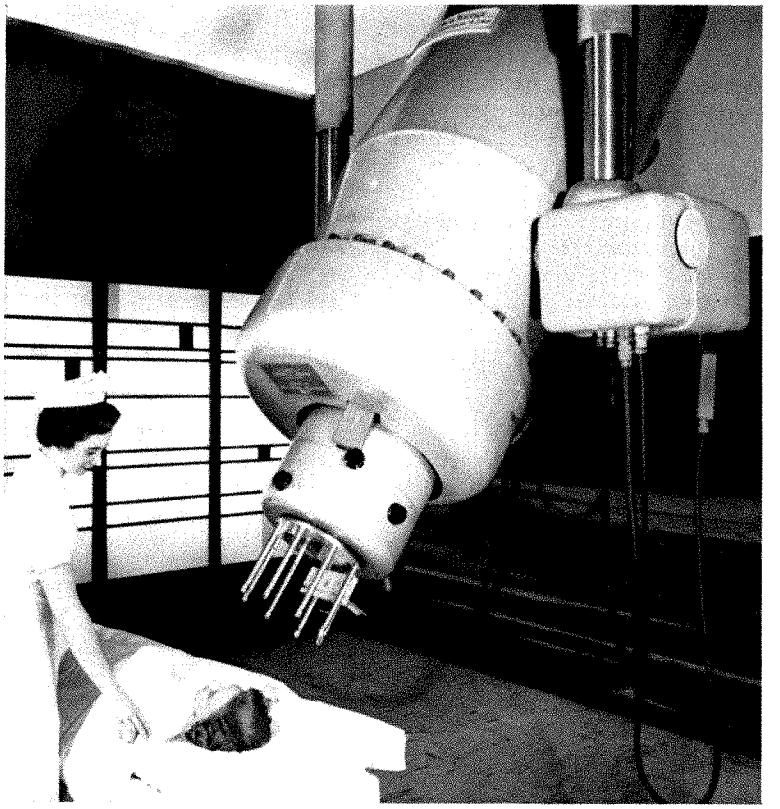
For a small hospital starting a diagnostic radioisotope laboratory with a small patient load and a modest budget, there is nothing quite as appropriate as a scanner. Hence, four out of five nuclear medicine departments get started with a Magnascanner and there are now over 2500 in use throughout the world. Similarily, a Magnascanner is a most relevant choice for larger hospitals in need of an instrument with the highest resolution for diagnostic confirmation. A basic scanner like the Magnascanner is still the best device available for static-imaging applications by virtue of its very high resolution, large field of view, wide energy range, contrast enhancement, wide choice of focusing collimators, and modest cost.

None of this should imply that the Magnascanner is an untouched island in the stream of progress. Today's instrument is generations away from yesterday's. Note: (1) maximum scan speed has been increased from 200 cm/min to 500 cm/min; (2) detector can be positioned by a control on the detector head itself, and a ratemeter on the detector head facilitates and speeds location of "hot" and "cold" spots; (3) a new color photo recording system is available in addition to black and white photorecording, multicolor dot recording, and Teledeltos black dot recording; (4) push button energy window selection (in addition to manual selection) for the most common radioisotopes used in diagnosis.

And Now the Dual Magnascanner®—This instrument is essentially identical to the Magnascanner® 500 except that it has two separate opposed detectors which acquire information independently. AP and PA, or RL and LL rectilinear scans can be performed simultaneously. This capability minimizes the need for patient re-positioning and reduces the scanning time by half.

Further information is available—Please write for detailed information on the Magnascanner® 500 and the Dual Magnascanner to Picker Nuclear, 1275 Mamaroneck Avenue, White Plains, N.Y. 10605. Please request file 235R.

PICKER

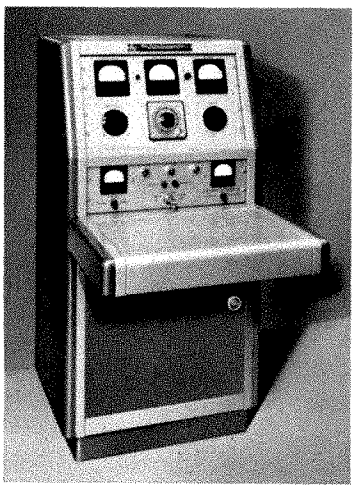


Improved Model AM Van de Graaff is the result of experience gained in 40 previous installations.

IMPROVED *Van de Graaff*® ACCELERATOR MEETS THE MODERN NEED FOR LOW-COST PRECISION THERAPY

Today's Model AM 2 MeV Van de Graaff Therapy Unit continues to keep pace with the trend to low-cost precision therapy in leading hospitals and cancer clinics throughout the Free World. And for five good reasons:

- Its less than 3 mm "point source" of x-rays allows optimum technics for both large and small treatment fields.
- Its treatment beam is accompanied by negligible penumbra.
- Its Roentgen output exceeds that of a 5000 curie cobalt source.
- Its x-ray output will not fall off. You can hold treatment techniques and parameters constant.
- It can be operated easily by a technician without a staff physicist in attendance.



The Model AM Van de Graaff is a reliable, proven source of high-energy radiation. It offers more roentgens-per-dollar and has demonstrated less overall cost-per-treatment than any other comparable supervoltage source available today — including radioisotopes.

Full time use of the reliable Model AM 2 MeV Van de Graaff Therapy Unit will amplify your technic range and expand your patient handling capacity. It is backed by the international reputation of the leading manufacturer of particle accelerators — High Voltage Engineering Corporation. Write Medical Sales.

Today's Model AM is routinely operated by an easily-trained technician.

HIGH VOLTAGE ENGINEERING CORPORATION
BURLINGTON, MASSACHUSETTS

GENERAL INFORMATION

Manuscripts offered for publication and other correspondence relating to the editorial management and books for review should be sent to Dr. Traian Leucutia, Editor, 401 Professional Building, Detroit, Michigan 48201. Contributions may be sent in foreign languages and will be translated if found acceptable. Original articles are published with the understanding that they are contributed exclusively to THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE.

A certain number of illustrations will be supplied free of cost; but special arrangements must be made with the Editor and Publisher for excess illustrations and elaborate tables.

Fifty reprints are furnished without charge to authors. Additional reprints may be purchased according to a scale of prices that accompanies galley proofs. As soon as each issue is printed, the type is destroyed except for reprint orders *in hand*. Reprint orders *must* be returned with corrected galley proof to the Editorial Office if additional reprints are desired.

Correspondence regarding subscriptions, advertisements, and other business relating to THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE should be addressed to Charles C Thomas, Publisher 301–327 East Lawrence Avenue, Springfield, Illinois 62703. (All requests to be submitted in writing.)

Manuscripts should be typewritten, with double spacing, and good margins (not on thin paper) and the *original* should be sent to the Editor. The author should keep a carbon copy, as the original is not returned. The name of the author should appear on each sheet of manuscript. Tabular materials should be typed on separate sheets; likewise bibliographical lists, footnotes, etc.

Drawings and charts for reproduction should be made in black (*never* in blue). Photographic prints of plates or slides on glossy paper produce the best half-tones.

All photographs and drawings intended for illustrations should be numbered, the top plainly indicated, and an abbreviated title of the paper placed on the back of *each one*.

Legends for illustrations should be typewritten in a single list, double spaced, with numbers corresponding to those on the photographs and drawings, instead of attaching each legend to its corresponding figure.

Care in preparation of bibliographies will save much time and correspondence. Each reference in a bibliography should include the following information in the order indicated: Name of the author with initials; title of the article; name of the periodical; year, volume and pages. It is requested that the authors use the following as model:

1. Olcott, C. T., and Dooley, S. W. Agenesis of lung of infant. *Am. J. Dis. Child.*, 1943, *65*, 766–780.

The month should be given if the reference is to an issue of the current year. An alphabetical arrangement of the authors is requested.

The author should always place his full address somewhere on his manuscript. This is very important and is often omitted.

For information regarding membership in the American Roentgen Ray Society, address the Chairman of the Executive Council, Dr. E. F. Van Epps, Duke University, Durham, North Carolina 27706.

For information regarding the program of the annual meeting of the American Roentgen Ray Society, address the President-Elect, Dr. James C. Cook, LL 14 Professional Plaza, 3790 Woodward Avenue, Detroit, Michigan 48201.

For information regarding membership in the American Radium Society, address the Secretary, Dr. John V. Blady, The Parkway House, 2201 Benjamin Franklin Parkway, Philadelphia, Pennsylvania 19130.

For information regarding the program of the annual meeting of the American Radium Society, address the President, Dr. Juan A. del Regato, Penrose Cancer Hospital, 2215 North Cascade Avenue, Colorado Springs, Colorado 80907.

THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE is owned, maintained by, and in the interests of the American Roentgen Ray Society, Inc. It is issued monthly by Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Illinois 62703. THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE does not hold itself responsible for any statements made or opinions expressed by any contributors in any article published in its columns.

Delivery is not guaranteed. Replacements are not guaranteed nor promised, but will be attempted if extra single copies are available and only if requested within 30 days from first of month following publication (17th of month) for domestic subscribers and 60 days for foreign subscribers.

Annual subscription price is as follows: United States, U. S. Possessions, U. S. Trusteeships, Pan-American Union, and Canada, $20.00; other countries $22.00. Prices for back volumes quoted on application. Extra single copies of back issues, if available, $2.00, postpaid. Current subscriptions may begin with any issue. Remittance should be sent to CHARLES C THOMAS, PUBLISHER, 301–327 East Lawrence Avenue, Springfield, Illinois 62703, U.S.A.

ADDRESS CHANGE—When a change of address is necessary please allow at least 60 days notice and preferably 90 days. When ordering a change of address, send the Publisher both the old and new address.

Entered as Second-class at Springfield, Illinois under the Act of March 3, 1879. Printed in U.S.A.
Second-class postage paid at Springfield, Illinois and at additional mailing offices.

Copyright © 1969, by AMERICAN ROENTGEN RAY SOCIETY, Inc. No part may be duplicated or reproduced without permission of both the Publisher and the Editor.

THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE

VOL. 105 MARCH, 1969 NO. 3

TABLE OF CONTENTS

The Centralization of Cancer Services—How Far Should It Go?; The Janeway Lecture, 1968. W. G. COSBIE, M.B. 487

The Value of Radiotherapy in the Management of Esophageal Cancer. J. G. PEARSON 500

Some Opinions on Treatment of Cancer of the Esophagus. W. D. RIDER, M.B., AND R. DIAZ MENDOZA, M.D. 514

Dosimetric Considerations in Cobalt 60 Rotational Therapy for Esophageal Lesions; A Comparison of Transit and Intraluminal Dose Measurement. DAVID B. GOLDENBERG, M.D., U. V. GOPALA RAO, ScD., STEWART LOTT, M.D., AND JOSEPH DIGEL, R.T. 518

Surgical and Radiation Treatment of Cancer of the Thoracic Esophagus. JOHN T. GOODNER, M.D. 523

Radiation Induced Neoplasia Following External Beam Therapy for Children with Retinoblastoma. ROBERT H. SAGERMAN, M.D., J. ROBERT CASSADY, M.D., PATRICIA TRETTER, M.D., AND ROBERT M. ELLSWORTH, M.D. 529

The Influence of the Relationship "Local Tumor Extent-Time" Upon the Evolution of Tumors of the Nasopharynx. J. F. BOHORQUEZ, M.D. 536

Radiation Therapy of Carcinoma of the Anterior Nasal Cavity. WAYNE P. WHITCOMB, M.D. 550

Hydroxyurea: A Radiosensitizer in the Treatment of Neoplasms of the Head and Neck. GEORGE J. RICHARDS, JR., M.D., AND ROBERT G. CHAMBERS, M.D. 555

Long Time Survivals of Patients with Cancer of the Eye and Surrounding Structures Treated with Radiation Therapy. CHARLES L. MARTIN, E.E., M.D. 566

An Evaluation of the Manchester System of Treatment of Carcinoma of the Cervix. GEORGE SCHWARZ, M.D. 579

The Combination of External Irradiation and Curietherapy Used Preoperatively in Adenocarcinoma of the Endometrium. VICTOR A. MARCIAL, JOSÉ M. TOMÉ, AND JEANNIE UBIÑAS 586

(*Continued on page iv*)

Recurrent Cancer of the Corpus Uteri; Techniques and Results of Treatment. AHMED O. BADIB, M.D., SAMUEL S. KUROHARA, M.D., ANTONIO A. BEITIA, M.D., AND JOHN H. WEBSTER, M.D., ... 596

Adenocarcinoma of the Uterus. LUIS DELCLOS, M.D., GILBERT H. FLETCHER, M.D., AUGUSTO G. GUTIERREZ, M.D., AND FELIX N. RUTLEDGE, M.D. 603

Afterloading Vaginal Ovoids. ALLAN E. GREEN, JR., M.D., JOHN R. BROADWATER, M.D., AND JAMES A. HANCOCK, JR., MAJOR, USAF, B.S.C. . 609

The Role of Preoperative Irradiation in the Treatment of Carcinoma of the Ovary. JEROME M. VAETH AND FRANZ J. BUSCHKE 614

The Clinical Course of Hodgkin's Disease and Other Malignant Lymphomas Treated with Radical Radiation Therapy. LEONARD R. PROSNITZ, M.D., SAMUEL HELLMAN, M.D., CARL F. VON ESSEN, M.D., AND MORTON M. KLIGERMAN, M.D. 618

Curative Treatment of Hodgkin's Disease. JOHN F. HYNES, M.D. 629

Cutaneous Reactions after Radiation Therapy; Report of 7 Cases. WILLIAM S. MAXFIELD, M.D., AND WILLIAM P. COLEMAN, M.D. 636

Dystrophic Epidermolysis Bullosa; Tolerance of the Bed and Response of Multifocal Squamous Cell Carcinomas to Ionizing Radiation: Report of a Case. ROBERT W. EDLAND, M.D. 644

A Light Analog System for Radiotherapy Planning. GERALD S. FREEDMAN, B.M.E., AND PAUL N. GOODWIN, PH.D. 648

Radiation Tolerance of the Thoracic Spinal Cord. THEODORE L. PHILLIPS, M.D., AND FRANZ BUSCHKE, M.D. 659

Changing Perspectives in Oxygen Breathing and Radiation Therapy. PHILIP RUBIN, M.D., COLIN A. POULTER, M.B., AND RAYMOND S. QUICK, B.Sc. 665

Isotope Renography and Renal Arteriography in the Evaluation of Renal Transplants. HAROLD D. DAVIDSON, M.D., MERLE K. LOKEN, PH.D., AND KURT AMPLATZ, M.D. 682

The Plugging of Leaks in Radium Containers. M. L. ROZENFELD, M.S., AND E. W. MASON, B.S. 689

Officers 698

Editorial

The Reynolds Historical Library. TRAIAN LEUCUTIA, M.D. 699

News Items 702

Book Review 703

Books Received 703

Society Proceedings 705

Abstracts of Radiological Literature 711

"prep" the colon with pleasant-tasting X-PREP Liquid

(standardized extract of senna fruit)

Specifically designed for preradiographic bowel evacuation, X-PREP Liquid permits excellent visualization in G.I. and urologic roentgenography.

No significant gas shadows. No residual oil droplets.

X-PREP Liquid reduces or eliminates the need for enemas prior to radiography.

And delicious X-PREP Liquid gives a welcome reprieve for your patients from the obnoxious taste of castor oil.

Easy-to-take, X-PREP Liquid is also easy to administer. Premixed and premeasured, this effective bowel evacuant comes in small, single-dose bottles—to be taken between 2 and 4 p.m. on the day prior to radiography. Patients should be advised to expect strong purgative action.

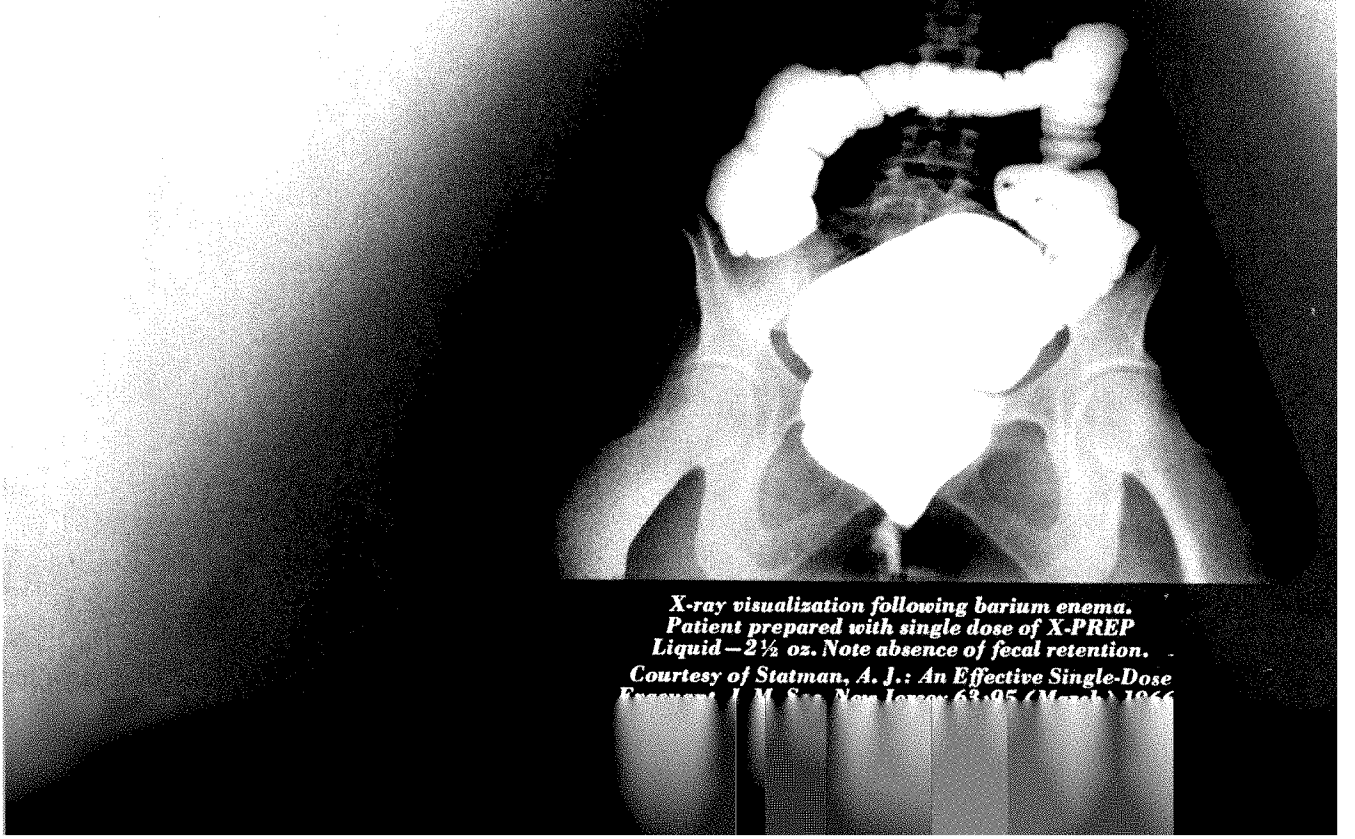
Contraindication: Acute surgical abdomen.
Supplied: Ready-to-drink in 2½ oz. bottles (complete adult dose).
Also available: X-PREP Powder (standardized senna concentrate). Mixed with water, ¾ oz. canister provides complete adult dose.

GRAY PHARMACEUTICAL CO., AFFILIATE,
THE PURDUE FREDERICK COMPANY,
Yonkers, New York

© COPYRIGHT 1968, GRAY PHARMACEUTICAL CO. E-25168R

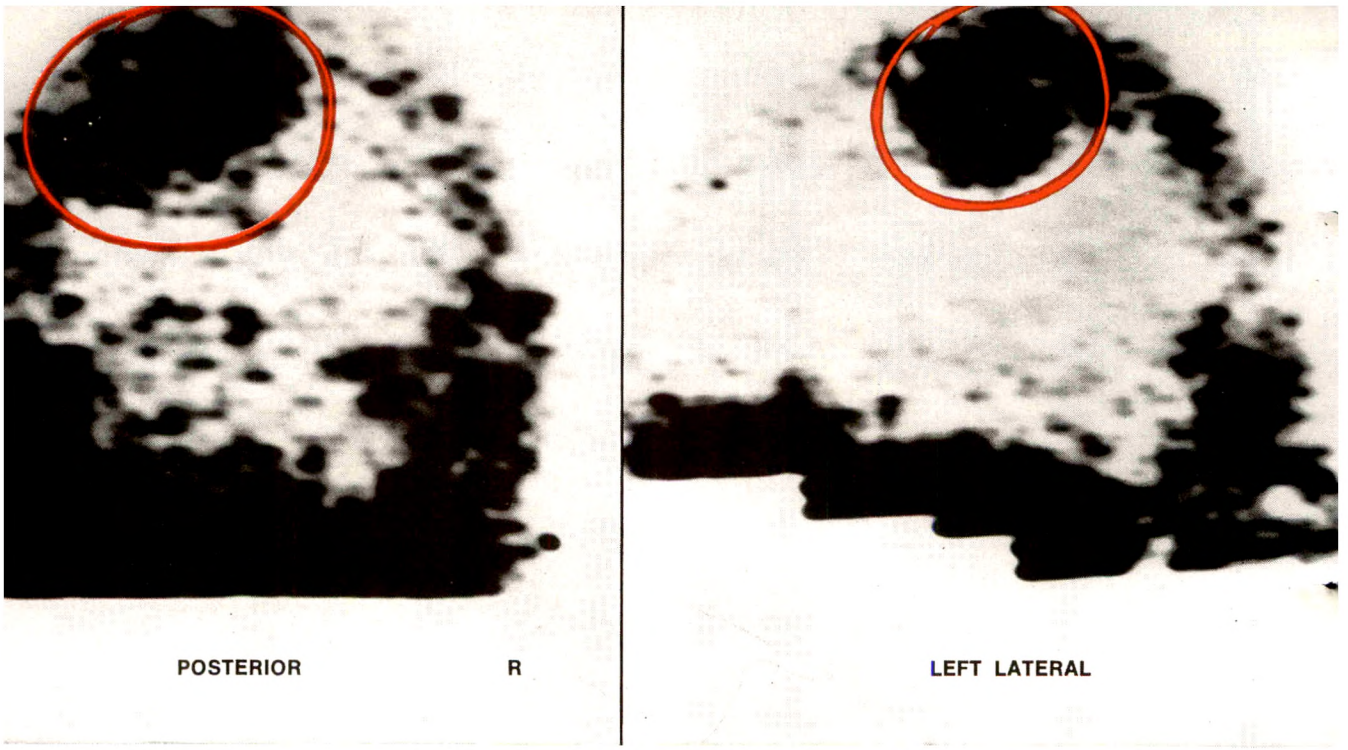


for a clear picture



X-ray visualization following barium enema. Patient prepared with single dose of X-PREP Liquid—2½ oz. Note absence of fecal retention.

Courtesy of Statman, A. J.: An Effective Single-Dose



POSTERIOR R

LEFT LATERAL

In suspected brain pathology, find out fast with **Pertscan**-99m

For brain scanning, Pertscan-99m provides more information with less radiation to the patient than any other related cerebral test—whether other radioisotopes or x-rays. And you get each projection fast—as little as 2 minutes with a camera, 15 minutes or less with rectilinear scanners.

A 54-year-old man was hospitalized with progressive weakness of the right side, followed by seizures of the right side (Jacksonian seizures). Brain scans showed an abnormal concentration of isotope in the left parasagittal area. Surgery revealed a meningioma, which was removed, and the patient recovered.

The 2 scans above, showing the marked abnormal uptake (which turned out to be a meningioma), were made with Pertscan-99m. This product is shipped Monday through Friday—and Sunday. Thus, brain scans can be scheduled 6 days a week—Monday through Saturday.

INDICATIONS: Adjunctive diagnostic aid in detecting and localizing intracranial neoplastic (primary or metastatic) and non-neoplastic lesions.

CONTRAINDICATIONS: Radio-pharmaceutical agents should not be administered to pregnant women or to persons less than 18 years old unless the indications are very exceptional.

PRECAUTIONS: Care should be taken to ensure minimum radiation exposure to the patient as well as all personnel; to prevent extracranial contamination because this can lead to erroneous interpretation; and to differentiate areas of abnormal activity from areas of normal vascular activity.

Pertscan™-99m
SODIUM PERTECHNETATE Tc 99m

Also available:

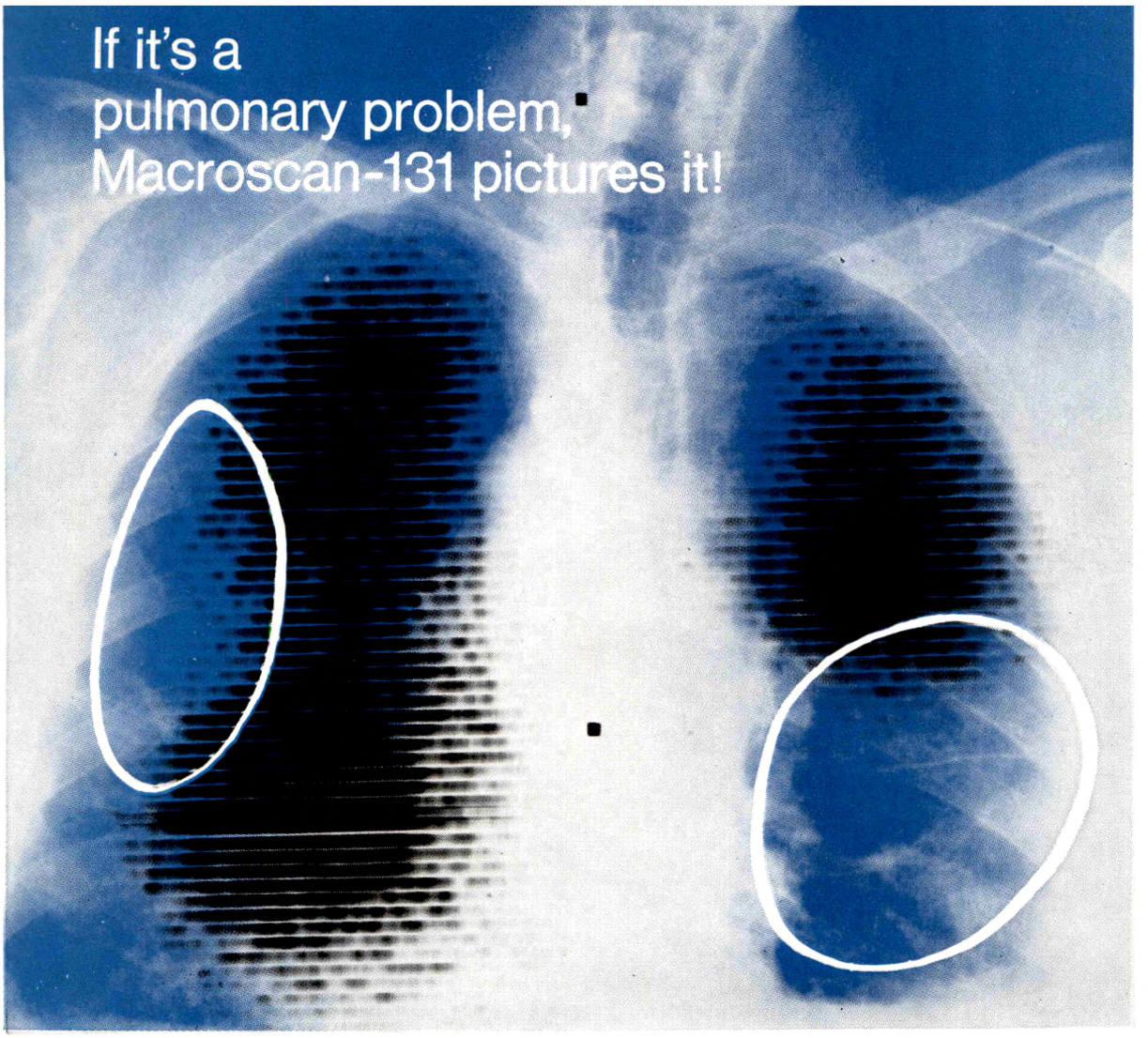
Pertgen™-99m
TECHNETIUM 99m GENERATOR KIT

ABBOTT LABORATORIES NORTH CHICAGO, ILLINOIS

Abbott Laboratories, S.A., 2, rue Thalberg, 1201 Geneva, Switzerland

™—Trademark

804464



A 70-year old man was admitted unconscious to the intensive care unit. Studies failed to reveal evidence of a myocardial infarction and the X-ray was not revealing. A pulmonary infarct was suspected and this diagnosis was established by a lung scan.

His posterior view scan above, showing diminished uptake in the left lingula and right lower lobe, was made with Macroscan-131. This product has many diagnostic uses:

Pulmonary embolism, suspected: To confirm (or rule out) its occurrence.

Chronic pulmonary tuberculosis: To estimate unilateral and regional function and perfusion of the lungs.

Emphysema: To evaluate the decreased regional blood flow that occurs with obstruction of vessels.

Pneumonitis: To evaluate the decreased regional blood flow that occurs without obstruction of vessels.

Lung Tumors: To evaluate the regional ischemia resulting from compression or obstruction of pulmonary arteries.

Surgery and/or other therapy for lung disorders: To evaluate the effectiveness of therapeutic measures.

Macroscan™-131

AGGREGATED RADIO-IODINATED (I^{131}) ALBUMIN (HUMAN)

Macroscan-131 is sterile and non-pyrogenic. It is ready to use and should not be heated prior to use.

INDICATIONS: For scintillation scanning of the lungs to evaluate total, unilateral, and regional arterial perfusion of the lungs.

CONTRAINDICATIONS: Radio-pharmaceutical agents should not be administered to pregnant women or to persons less than 18 years old unless the indications are very exceptional.

PRECAUTIONS, SIDE EFFECTS: Care should be taken to administer the minimum dose consistent with safety and validity of data. The possibility of an immunological response to albumin should be kept in mind when serial scans are performed. There is a theoretical hazard in acute cor pulmonale, because of the temporary small additional mechanical impediment to pulmonary blood flow. A possible case of urticaria has been related to a similar preparation. The thyroid gland should be protected by prophylactic administration of concentrated iodide solution. 903116

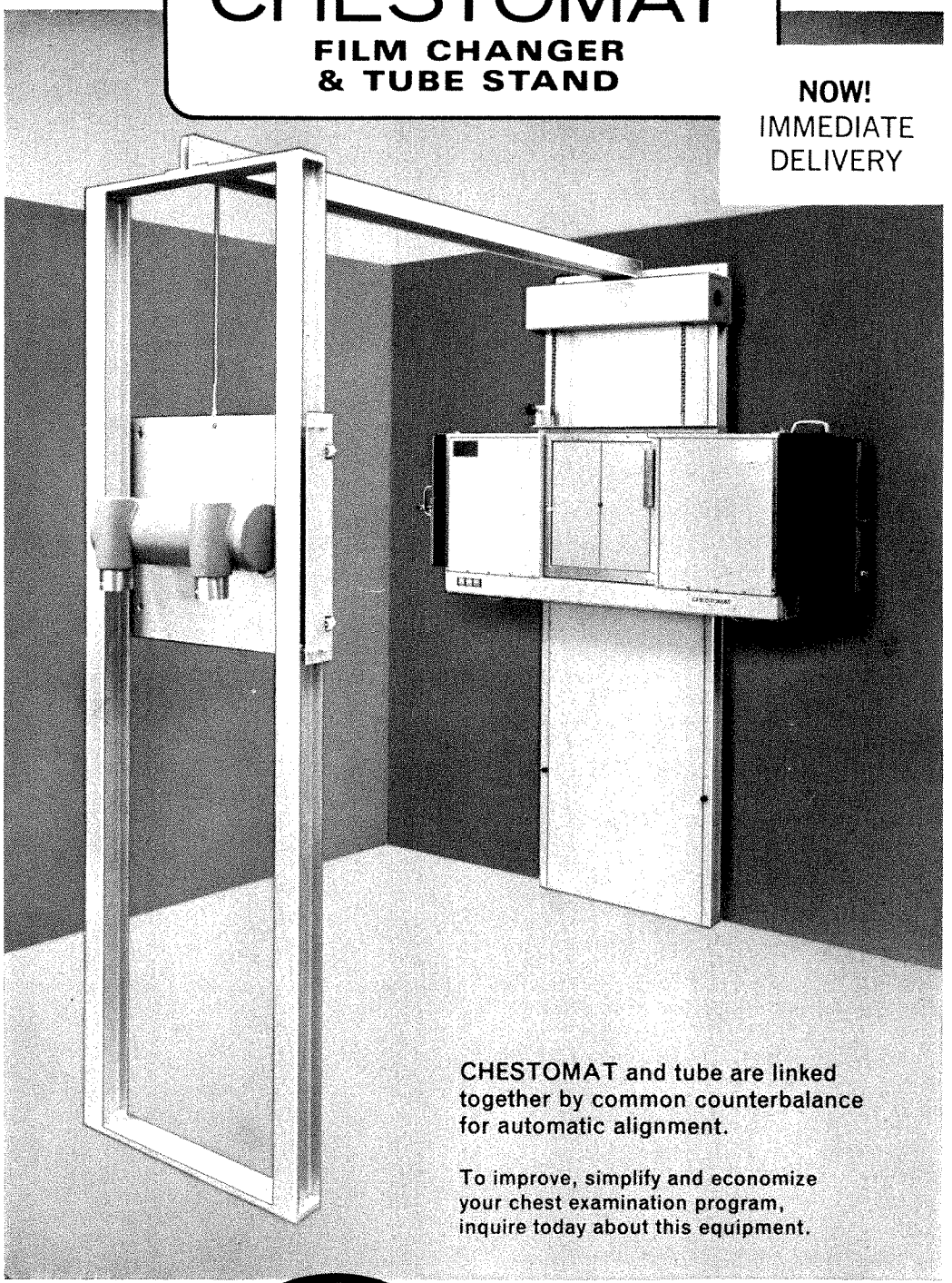
ABBOTT LABORATORIES
North Chicago, Illinois 60064

World's Leading Supplier of Radio-Pharmaceuticals
LABOR-SERVICE GMBH, Abteilung RADIO-PHARMAZEUTIKA,
6236 Eschborn/Ts, Frankfurter Str. 20, Postfach 1245

CHESTOMAT

FILM CHANGER & TUBE STAND

NOW! IMMEDIATE DELIVERY



CHESTOMAT and tube are linked together by common counterbalance for automatic alignment.

To improve, simplify and economize your chest examination program, inquire today about this equipment.

SCHICK X-RAY

SCHICK X-RAY CO., INC.

415 Green Bay Road • Wilmette, Illinois 60091

Phone (312) 256-4700

WHEN YOUR SPECIALTY IS ROENTGENOLOGY

17 Books Selected from the Thomas Catalog of over 2100 Titles . . .

☐ **THE CARE OF RADIATION CASUALTIES** *by* **John Blakely,** *Medical Officer-in-Charge, United Kingdom Atomic Energy Authority.* '68, 136 pp., 17 il. (1 in color), 10 tables, $5.50

☐ **SELECTIVE RENAL ARTERIOGRAPHY: Its Application to the Diagnosis of Renal Vascular and Parenchymal Lesions** *by* **Ivan L. Bunnell,** *State Univ. of New York at Buffalo.* '68, 248 pp. (6¾ × 9¾), 183 il., $18.75

☐ **AN ATLAS OF PATHOLOGIC PNEUMOENCEPHALOGRAPHIC ANATOMY** *by* **Giovanni Di Chiro,** *National Institute of Neurological Diseases and Blindness, Bethesda, Md.;* **Mannie M. Schechter,** *Albert Einstein College of Medicine, New York City; and* **Ingmar Wickbom,** *Univ. of Gothenburg Medical School, Sweden.* '67, 594 pp. (11 × 8½), 926 il. (5 in color), $49.50

☐ **X-RAY DIAGNOSIS OF CONGENITAL CARDIAC DISEASE** *by* **Larry P. Elliott** *and* **Gerold L. Schiebler,** *both of Univ. of Florida College of Medicine, Gainesville. Foreword by* **Paul C. Hodges.** '68, 260 pp., 221 il., 3 tables, $11.50

☐ **PRINCIPLES OF RADIOGRAPHIC EXPOSURE AND PROCESSING (2nd Ed., 5th Ptg.)** *by* **Arthur Fuchs,** *Rochester, N.Y.* '68, 304 pp. (7 × 10), 600 il., $11.00

☐ **FUNDAMENTAL PROBLEMS IN SCANNING** *compiled and edited by* **Alexander Gottschalk** *and* **Robert N. Beck,** *both of Univ. of* Chicago. *(38 Contributors)* '68, 424 pp. (7 × 10), 309 il. (10 in full color), 12 tables, $26.75

☐ **ROENTGENOGRAPHIC DIAGNOSIS OF BLADDER TUMORS** *by* **Erich K. Lang,** *Methodist Hosp., Indianapolis.* '68, 132 pp. (7 × 10), 94 il., 11 tables, $9.75

☐ **HODGKIN'S DISEASE** *compiled and edited by* **David W. Molander,** *Cornell Univ. Medical College, and* **George T. Pack,** *New York Medical College. Both of New York City. (7 Contributors)* '68, 228 pp. (7 × 10), 121 il., 39 tables, $15.00

☐ **AIDS TO ETHICS AND PROFESSIONAL CONDUCT FOR STUDENT RADIOLOGIC TECHNOLOGISTS (2nd Ed.)** *by* **James Ohnysty,** *St. Francis Hosp., Colorado Springs.* '68, 172 pp., $6.75

☐ **ROENTGENOLOGY OF THE SPLEEN AND PANCREAS** *by* **Josef Rosch,** *Charles Univ., Prague, Czechoslovakia.* '67, 376 pp. (6¾ × 9¾), 434 il., $29.75

☐ **SOLITARY METASTASES** *by* **Philip Rubin,** *Univ. of Rochester Medical Center, New York, and* **Jerold Green,** *Zellerbach Saroni Tumor Institute, Mt. Zion Hosp., San Francisco.* '68, 268 pp., 153 il., 30 tables, $14.75

☐ **CANCER THERAPY BY INTEGRATED RADIATION AND OPERATION** *compiled and edited by* **Benjamin F. Rush, Jr.,** *and* **Robert H. Greenlaw,** *both of Univ. of Kentucky College of Medicine, Lexington. Foreword by* **Charles Tucker.** *(40 Contributors)* '68, 176 pp. (7 × 10), 58 il., 82 tables, $12.75

☐ **LUNG CALCIFICATIONS IN X-RAY DIAGNOSIS** *by* **Emanuel Salzman,** *Univ. of Colorado School of Medicine, Denver.* '68, 132 pp. (6¾ × 9¾), 74 il., $7.50

☐ **THE FUNDAMENTALS OF X-RAY AND RADIUM PHYSICS (4th Ed., 5th Ptg.)** *by* **Joseph Selman,** *Univ. of Texas, Tyler.* '69, 498 pp., 306 il., 16 tables, $10.50

☐ **CERVICAL SPONDYLOSIS AND ITS NEUROLOGICAL COMPLICATIONS** *by* **Bernard H. Smith,** *State Univ. of New York at Buffalo.* '68, 240 pp. (6¾ × 9¾), 101 il., $12.00

☐ **NORMAL RADIOLOGICAL ANATOMY: Radiological Optics and Film Interpretation** *by* **Henry Tillier,** *Late Professor of Radiology, Algiers. Translated and edited by* **Ronan O'Rahilly,** *St. Louis Univ. School of Medicine.* '68, 400 pp., 375 figs., 3 tables, $12.50

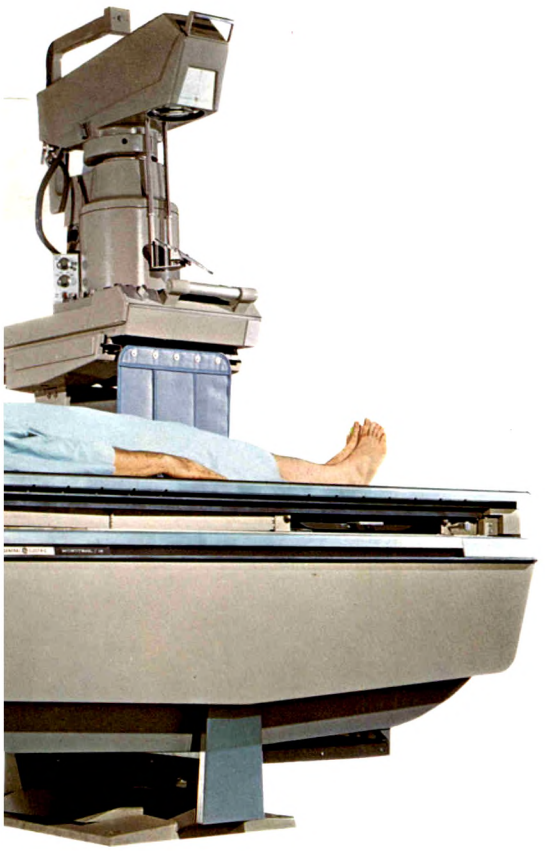
☐ **ADVANCES IN DYNAMIC RADIOACTIVE SCANNING** *compiled and edited by* **Yen Wang,** *Univ. of Pittsburgh, Pa. (10 Contributors)* '68, 140 pp., 101 il., 7 tables, $8.50

CHARLES C THOMAS • PUBLISHER 301-327 East Lawrence Ave. **SPRINGFIELD • ILLINOIS • 62703**

DIAGNOSTIC X-RAY GENERATORS



From the Power People



Consistency without Compromise. Whatever your procedure, whatever your technic, there is a definite power range you require for the best diagnostic result. That's why General Electric offers the broadest line of diagnostic x-ray generators in the industry. Once you determine your procedural requirements, your GE sales representative will recommend the generator to best suit your needs. In fact, he will work with you, providing knowledgeable suggestions to assure maximum efficiency without compromise.

Variety in generator models is only a part of the GE generator story. Precision design and manufacturing is the real key to consistently excellent results. Our energy conversion experts are sticklers for detail and insist that every component part of every GE generator does its job to perfection. Results are consistent because power output is consistent.

When planning your next x-ray installation, let your GE sales representatives and service technicians take total responsibility for providing you with an equipment-matched power system. The finely tuned system you receive will rarely need service. When it does, the service will be fast and efficient because every GE generator is built with fast access swing-out panels for serviceability.

For consistent results free of procedural compromise and the finest service available call on General Electric —the power people.



Progress is our most important product

GENERAL ELECTRIC

X-RAY DEPARTMENT • MILWAUKEE, WISCONSIN 53201

←NOW AVAILABLE→

CONSOLIDATED INDICES

VOLUME VI

embracing

The American Journal of Roentgenology, Radium Therapy and Nuclear Medicine

Volumes 79-88 (1958-1962)

Covers some 8,000 pages of original papers, editorials, biographical sketches, and abstracts of both domestic and foreign journals published in THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE for the years 1958-1962.

Fills a very definite need and will be welcomed by those who have occasion to consult the Journal during this five-year period. Increases the usefulness of your set of journals a hundred-fold.

A Limited Quantity Has Been Printed

Order Your Copy NOW

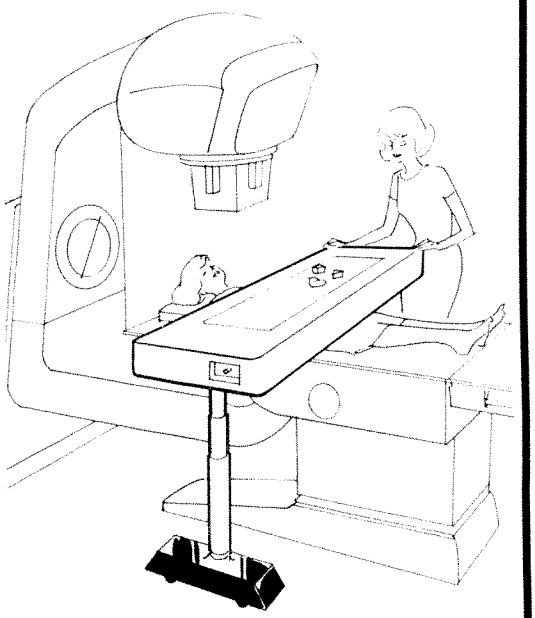
CHARLES C THOMAS · PUBLISHER
301-327 East Lawrence Avenue
Springfield · Illinois

Send me the volumes I have checked below. I understand that orders are subject to the exhaustion of available stock. (This order is subject to withdrawal without notice.)

Volume II (1938-1942), $10.00
Volume III (1943-1947), $22.50
Volume IV (1948-1952), $23.50
Volume V (1953-1957), $25.00
Volume VI (1958-1962), $23.50
*Volume I (1903-1937) out of print.

name .....
address .....
city ..... zone .....
state .....

new from BARUCH



Three new products to shorten radiation therapy set-up time . . . Contribute to the highest standards of patient care.

The BeamBlock Table is an adjustable, free-moving table for positioning lead beam-trimming blocks. Eliminates awkward and time-consuming clamps, since blocks rest on table, are not fastened to therapy unit. Special features: see-thru window, block supports for angled shots.

The BeamBlock Stand is an adjustable, mobile stand for positioning a lead shielding block. Equally convenient, whether patient is lying down or sitting up—and particularly adaptable for head and neck treatments.

We have a full range of standard block sizes available for both units.

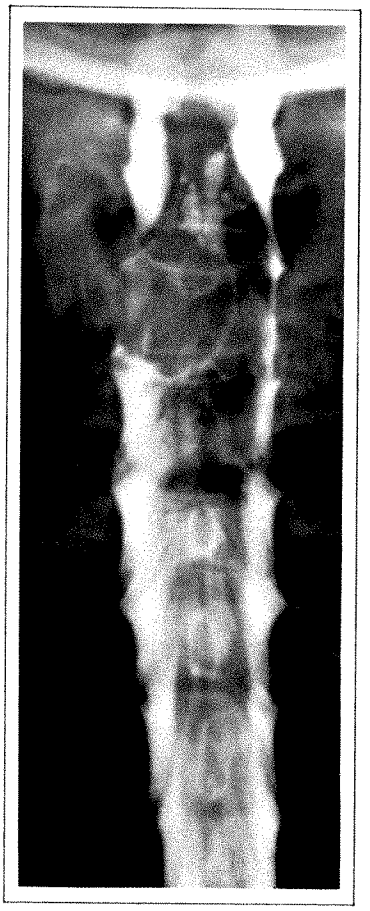
The Variangle Cassette Holder brings the film to the patient for field verification and localization shots. Facilitates angled shots. It is a flexible, moveable stand which positions standard film cassettes and has an economy feature: the Cassette Holder arm is available as an accessory to the BeamBlock Stand.

Ask us for literature describing these and other accessories for radiation therapy—Baruch specializes in solving your therapy equipment problems.

BARUCH INSTRUMENTS CORPORATION
203 North Highland Avenue
Ossining, New York 10562
(914) 762-2255

The cervical myelogram illustrated here is an interesting demonstration of a relatively large neurofibroma in the spinal canal at the level of the third cervical vertebra.

During the first manipulation of Pantopaque® contrast medium into the cervical subarachnoid space, image of the column of contrast material was interrupted at the C-3 level, particularly on the right, and gave a first impression of the presence of a nonencapsulated, infiltrating, intramedullary tumor, which appeared to enlarge the spinal cord. On further manipulation, caudally, however, a thin stream of contrast material diverged to the left and outlined medial, upper, and lower borders of a well-circumscribed tumor.



The patient, a 58-year-old woman, had had cramping of the foot muscles, especially on the right, for about three years. Eight months prior to examination, she began to experience dull pain in the back of the head and stiffness of the lower limbs when descending stairs. About two months prior to myelography, she began to notice "pins and needles" sensations in all limbs, again particularly on the right, and developed difficulty in using her right upper limb.

The tumor was excised following laminectomy of the third, fourth, and fifth vertebrae and the spinal cord was thoroughly decompressed. The patient did very well postoperatively and today is an essentially well woman.

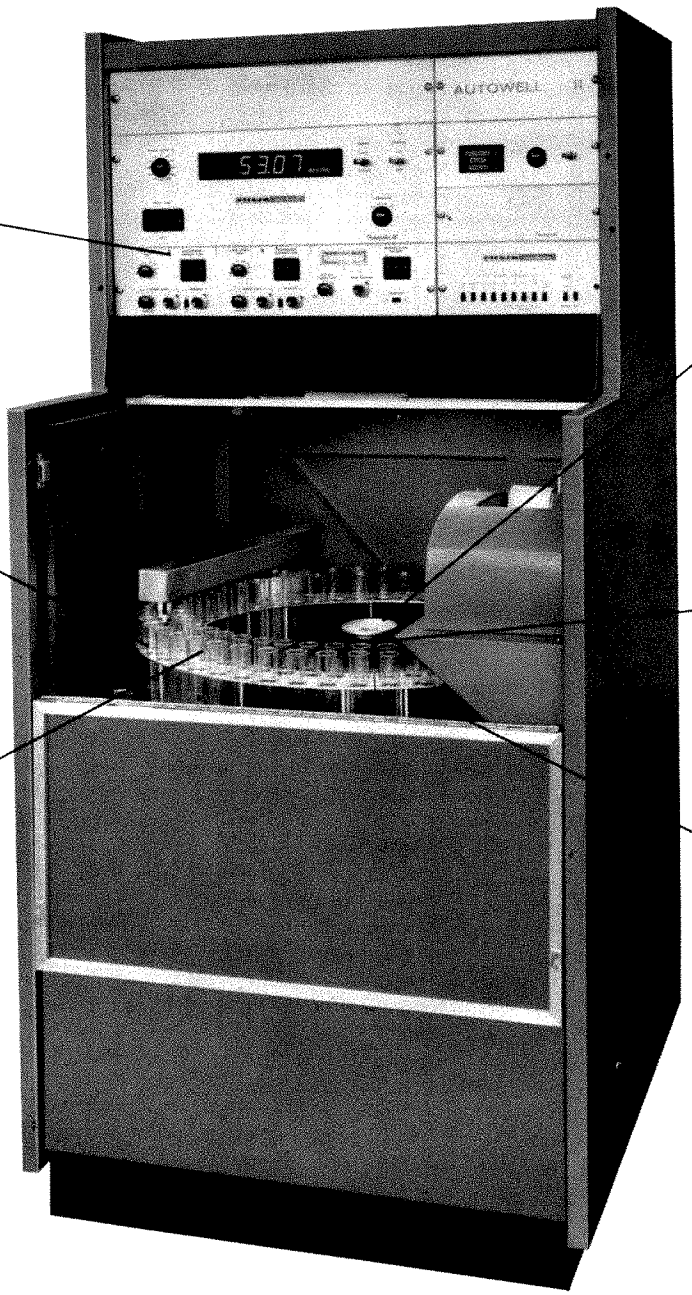
Side Effects. Clinical reports indicate that the incidence and the severity of the side effects following Pantopaque myelography with aspiration of the medium is but slightly greater than with ordinary lumbar puncture. In 10-30 percent of such cases there may be transient symptomatic reactions consisting of slight temperature elevation and increase of symptoms referable to a back condition. When the medium is not removed, similar transient side effects occur with a slight elevation of temperature in a greater percent of patients. To reduce the reactions to a minimum and to facilitate the absorption of the medium, the bulk of the Pantopaque should be removed by aspiration after myelography.

Contraindications. Pantopaque should not be injected where a lumbar puncture is contraindicated, nor within 10 days of a previous lumbar puncture. The latter precaution is necessary to avoid subdural and extra-arachnoid extravasation. An injection should not be carried out until the operator is certain that his needle is in the subarachnoid space.

Limitations. Pantopaque has not been studied adequately from a clinical standpoint as a contrast medium for body cavities other than the subarachnoid space. The limitations and contraindications in other areas are not known.

Pantopaque, the trademark under which all leading x-ray dealers supply the compound ethyl iodophenylundecylate, is prepared as the myelographic contrast medium Iophendylate Injection, U.S.P. by Lafayette Pharmacal Inc., Lafayette, Indiana 47904. Pantopaque is a registered trademark of Eastman Kodak Company.

Anatomy of an automatic gamma counting system.



The Picker Autowell® II

Actually the Picker Autowell® II is not a single system. Rather, the name designates an entire family of high efficiency systems that automatically count as many as 100 liquid or solid gamma-emitting samples in test tubes. You select the Autowell II that meets your individual requirements by choosing—from a wide selection—the detect scaler and printer that satisfy your particular needs. Wr for details to Picker Nuclear, 1275 Mamaroneck Avenu White Plains N.Y. 10605. Please request file 236R.

PICKER

SQUIBB

a research concept in contrast visualization

for better definition of disease: documenting differences between contrast agents

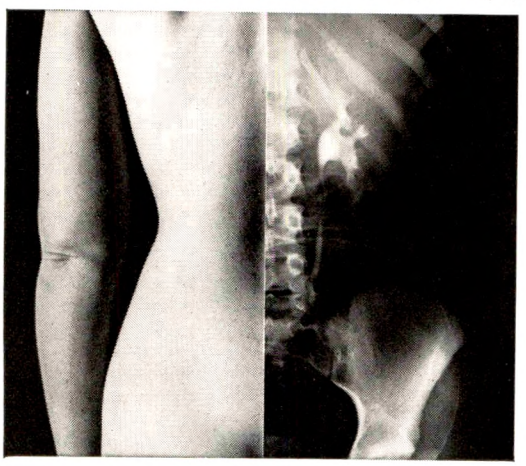
No. 1 in a series:

Renografin-60 (meglumine diatrizoate injection) preferred in a study of pyelographies of 2,234 patients.

In a new large scale study,[1] "...to determine which medium would produce adequate visualization of the urinary tract with the fewest toxic effects on the patient," Macht *et al.* have compared Renografin-60 with 2 other contrast agents.

Data were analyzed in 2,234 unselected (consecutive) patients, according to age, sex, and general disease group for the study population as a whole. The first 683 patients received 50% diatrizoate sodium solution, the next 921 patients received Renografin-60, and the final 630 patients received 66.8% sodium iothalamate solution.[1]

criteria for quality and comparative safety The contrast agents were evaluated for quality of diagnostic films as follows: films showing a dense concentration of contrast medium with filling and visualization of all major and minor calyces, infundibula, pelves and almost all of each ureter were listed as "good"; films showing less concentration with incomplete visualization of all portions of urinary tract but sufficient to produce diagnostically adequate films were listed as "fair"; films showing unsatisfactory visualization of urinary tract, or films which could not be interpreted, as "poor." The media were also evaluated as to incidence of the following side effects: nausea, vomiting, fainting, shock or severe reaction, hiccups, hives, pain in arm, sneezing, hot flushes, stuffiness of nose or ears.[1]



The following chart* shows comparative results of the 3 media according to age category:

quality of pyelograms and side effects expected in standard population of 1,000 patients by age, according to type of medium used

medium used and type of patient	standard population	quality of pyelograms good	fair	poor	with side effects
meglumine diatrizoate					
all ages,	1,000	827	123	50	41
0-19†	126	122	3	1	3
20-49	415	374	35	6	27
50-69	315	240	51	24	9
70 or older	144	91	34	19	2
diatrizoate sodium					
all ages,	1,000	782	134	84	72
0-19	126	115	6	5	7
20-49	415	378	26	11	40
50-69	315	227	64	24	19
70 or older	144	62	38	44	6
sodium iothalamate					
all ages,	1,000	883	81	36	54
0-19	126	122	4	0	7
20-49	415	393	20	2	29
50-69	315	269	32	14	13
70 or older	144	99	25	20	5

*Adapted from Macht[1] †In some patients in this age group, higher than recommended doses were used.

In theory: "The choice of contrast agent should ideally be individualized according to the age, sex, and disease group of the patient in order to obtain a high probability of complete visualization of the urinary tract with low probability of adverse side effects."[1]

In practice: "The choice is to be made...on the basis of the agent which gives the best concentration and the fewest side effects in the greatest number of patients regardless of age, sex, or disease category."[1]

In order of preference: Although Renografin-60 was not rated highest in all categories, the authors feel that their preference of the contrast media for intravenous pyelography would be: first, Renografin-60; second, sodium iothalamate; third, diatrizoate sodium.[1]

For brief summary of prescribing information, please refer to the end of this advertisement.

definition of safety...

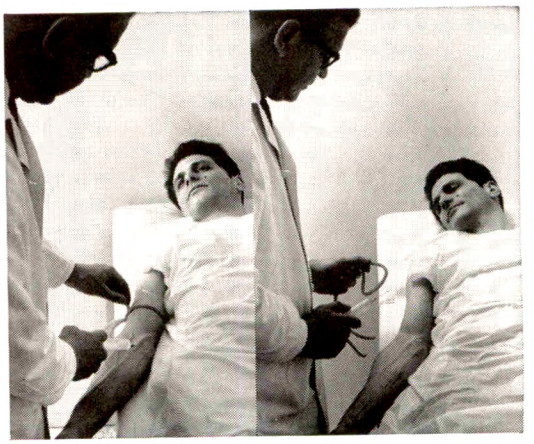
demonstrated in animals... Since meglumine diatrizoate is also used for cerebral angiography, toxicity studies of administration via the carotid artery are therefore of interest. Fischer and Eckstein[2] designed angiographic studies in animals in which procedures were very similar to clinical angiography, and which yielded data that was quantitative, graphic and nonsubjective.[2] According to the authors: "We selected the alterations in arterial blood pressure, venous pressure, heart rate and rhythm, the electrocardiogram and end-expiratory CO_2 concentration resulting from experimental cerebral angiography as refined, sensitive indications of the toxicity of a particular contrast material."[2] Their results of measured cardiovascular functions in dogs indicated that meglumine diatrizoate was far less toxic than four other contrast media.[2] As Fischer and Cornell reported in a later study: "Despite the testing of more highly concentrated solutions and larger doses, the cardiovascular responses [in dogs] from methylglucamine [meglumine] salts were much less than from sodium salts, an observation consistent with previous experiments."[3]

Other investigators have documented the comparative safety of meglumine salts in experimental studies. In order to determine reaction and tolerance of the intestines, Cooley[4] injected meglumine diatrizoate into mesenteric arteries of dogs and found no damage. Gensini *et al.*[5] reported that cardiovascular responses with it were almost identical to blood transfusions.

theory of lower toxicity with meglumine... Gensini and DiGiorgi have offered a hypothesis to explain their findings of lesser toxicity with experimental intravascular injections of methylglucamine (meglumine) salts. "When a relatively undiluted amount of sodium salts of a contrast agent is injected in an artery and carried by the blood stream toward the capillary bed, its molecules rapidly dissociate and readily diffuse through the capillary membrane and into the tissue. There, both the toxic effect of the iodine-containing organic radical and the increased concentration of sodium will readily manifest themselves. At equal concentrations of sodium, the end results will closely reflect the intrinsic toxicity of the iodine-containing organic radical on the tissues...."[5]

"In the case of the methylglucamine compounds, the same dissociation takes place. However the larger methylglucamine molecule, rich in hydrogen bonds, apparently either limits the migration of the organic radicals outside the vessel or at least minimizes their effects on the cellular metabolism."[5]

proved in practice... Paralleling similar findings in animals, clinicians have reported a generally lower



incidence of untoward reactions with Renografin-60 in urologic and cerebrovascular use. However, as with all intravascularly injected contrast agents, the possibility of severe reactions should be kept in mind (see Contraindications, Precautions and Side Effects below). In one study of over 600 urologic patients, the investigators reported that Renografin-60 produced urograms of diagnostic quality with a 6% incidence of side effects. The authors concluded: "It is hard to believe that any drug introduced intravenously could be so well borne by so many patients...."[6]

In a 74-patient study,[7] comparing Renografin-60 with diatrizoate sodium in carotid arteriography, Shealy commented: "With confused patients who are to have arteriography under local anesthesia, it is particularly desirable to have an agent that causes little pain." In this study, since "...60 per cent Renografin has resulted in considerably less pain than 50 per cent or 45 per cent [diatrizoate sodium]...we have converted to the routine use of 60 per cent Renografin for carotid arteriography; an additional 1,500 arteriograms done with 60 per cent Renografin have been quite satisfactory."[7]

better tolerated even in pediatrics... Citing some difficulties in administering contrast agents intravenously to children, Strasser *et al.*[8] selected Renografin-60 for intramuscular use in excretion urography in 16 pediatric patients because of the mild and relatively few reactions consistently associated with its use. The authors concluded: "The almost complete absence of any kind of local effect from its injection into the gluteal muscle and the absence of any serious reactions, local or systemic, indicate the safety of the medium."[8]

For brief summary of prescribing information please refer to the end of this advertisement.

definition of efficacy...

a thoroughly investigated meglumine salt Extensively evaluated for over a decade, Renografin has been consistently shown to yield a high percentage of diagnostic quality films in many phases of contrast visualization.

Upon intravenous injection, Renografin is rapidly carried to the kidneys and is so well concentrated that renal passages—including renal pelvis, ureters and bladder—may be clearly visualized. This medium also provides high contrast vasography in visualization of the cerebral vessels and the peripheral arteries and veins.

proved diagnostic excellence... In a comparative study[9] of 3 contrast agents used in cerebral angiography by Doehner (comprising a cross section of an average neurosurgical practice), Renografin-60 was equal in the arterial phase and slightly superior in the venous phase of the examination.

Findings of a previously cited study by Orr *et al.*,[6] in intravenous pyelography, also attest to the diagnostic excellence of Renografin-60. "Satisfactory roentgenograms of the kidneys were obtained in 636 (97%) of the cases, demonstrating the great diagnostic value of this procedure." And, as noted previously, Shealy found the contrast agent to be "quite satisfactory" in 1,500 carotid arteriograms.[7]

References: 1. Macht, S. H.; Williams, R. H., and Lawrence, P. S.: Amer. J. Roentgen. 98:79 (Sept.) 1966. **2.** Fischer, H. W., and Eckstein, J. W.: Amer. J. Roentgen. *86*:166 (July) 1961. **3.** Fischer, H. W., and Cornell, S. H.: Radiology *85*:1013 (Dec.) 1965. **4.** Cooley, R. N., *et al.*: Angiology *15*:107 (Mar.) 1964. **5.** Gensini, G. G., and DiGiorgi, S.: Radiology *82*:24 (Jan.) 1964. **6.** Orr, L. M.; Campbell, J. L., and Thomley, M. W.: J.A.M.A. *169*:1156 (Mar.) 1959. **7.** Shealy, C. N.: J. Neurosurg. *20*:137 (Feb.) 1963. **8.** Strasser, N. F., *et al.*: Radiology 79:408 (Sept.) 1962. **9.** Doehner, G. A., and Brugger, G. E.: New York J. Med. *60*:4022 (Dec.) 1960.

Contraindication

A history of sensitivity to iodine per se or to other contrast media is not an absolute contraindication to the use of meglumine diatrizoate.

Precautions and Side Effects

Severe, life-threatening reactions are rare; when they occur they suggest hypersensitivity. A personal or family history of asthma or allergy warrants special attention and may predict, more accurately than pretesting, the likelihood of a reaction, although not the type nor severity of the reaction in the individual.

The value of any pretest is questionable. The pretest most performed is the slow injection of 0.5-1.0 cc. of the preparation into a peripheral vein. An impending reaction is often indicated by transient burning and flushing, pain, "jump-like" reactions, respiratory difficulty, faintness, sneezing, itching, nausea, vomiting or urticaria. Should the test dose produce an untoward response, the necessity for continuing the examination should be re-evaluated. Antiallergic drugs may be used to advantage. In a few cases, the reactions to the test dose have been extremely severe.

The more serious anaphylactoid reaction requires immediate treatment and may occur despite a negative sensitivity test. An emergency tray consisting of vasopressor drugs, epinephrine hydrochloride 1:1000, methoxamine (Vasoxyl) or metaraminol bitartrate (Aramine), and glucose and saline is recommended. Oxygen and instruments to guarantee a clear airway must be readily available.

Caution must be exercised, especially in cerebral angiography in extreme age, in severely debilitated patients and in those with marked or severe hypertension, advanced arteriosclerosis, cardiac decompensation, recent cerebral embolism, or thrombosis, chronic pulmonary emphysema and in cyanotic infants.

For full details the Package Insert should be read.

Supply: Renografin-60 is supplied in vials and ampuls as a sterile aqueous solution providing 60% meglumine diatrizoate containing approximately 29% firmly bound iodine.

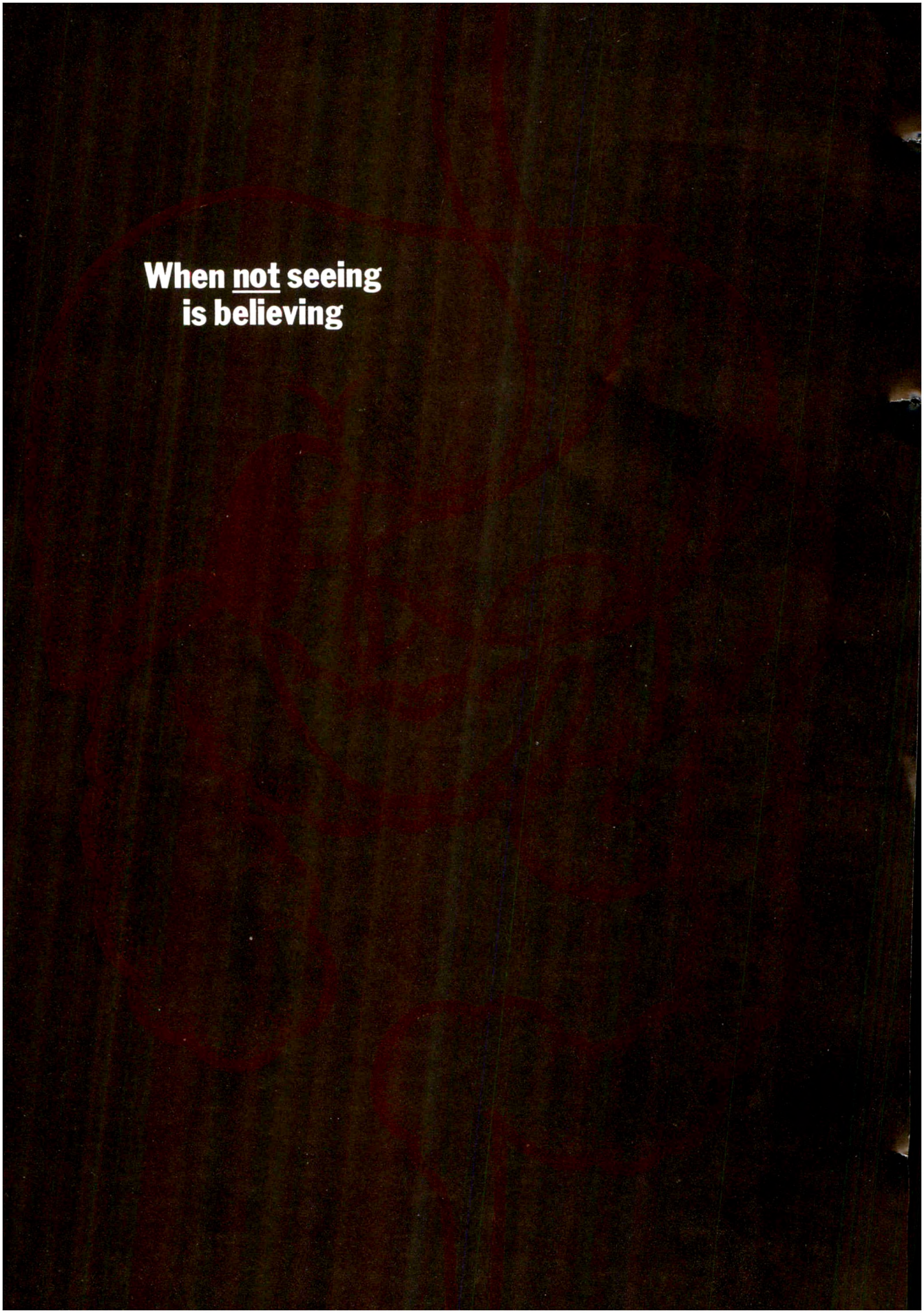
Available in 30 cc. vials or 25 cc. ampuls.

in excretion urography
cerebral angiography
peripheral arteriography
and venography

Renografin®-60

Squibb Meglumine Diatrizoate Injection U.S.P.

SQUIBB 'The Priceless Ingredient' of every product is the honor and integrity of its maker.


When not seeing
is believing

The full, precise visualization of the gallbladder obtained with TELEPAQUE is diagnostically important because it assures you that there is no cholecystic pathology. The fact that TELEPAQUE produces a complete picture proves the gallbladder is functioning normally.
But more important is the fact that TELEPAQUE, unlike other contrast agents, does *not* passively fill a diseased gallbladder. Thus the absence of visualization can be of great significance suggesting disease. With TELEPAQUE it is possible to detect those patients with cholecystitis who do not have stones. This indication of pathology, that TELEPAQUE provides adds to its reliability for diagnosis.

Use of TELEPAQUE in a series of 1,207 cholecystographic examinations resulted in 98.3% diagnostic accuracy.* TELEPAQUE has been used in more than 33,000,000 patients... an unparalleled record of tolerance.

Contraindications: Contraindicated in advanced hepatorenal disease or severe impairment of renal function, severe gastrointestinal disorders that prevent absorption, and in patients sensitive to iodine compounds.

Precautions: Severe, advanced liver disease may interfere with metabolism of Telepaque, thus increasing the excretory load on the kidneys. Although renal difficulty has rarely been attributed to Telepaque, renal function should be assessed before cholecystography in severe, advanced liver disease, and renal output and hepatic function should be observed for a few days after the procedure. Patients with preexisting renal disease should not receive high doses of cholecystographic media. Possible renal irritation in susceptible individuals could result in reflex vascular spasm with partial or complete renal shutdown. Caution is advised in patients with coronary disorders, especially those with recent symptoms of coronary artery disease. Blood pressure should be observed after administration of cholecystographic media to these patients. Elevation of protein-bound iodine for several months and false positive urine albumin tests (for three days) may occur after ingestion of iodine-containing cholecystographic media.

Adverse Reactions: Most reactions are mild and transitory; serious side effects are very rare. Gastrointestinal effects (diarrhea, cramps, nausea, vomiting) are the most common. Usually the diarrhea consists merely of a few loose stools, although in isolated cases it may be severe. A mild stinging sensation during urination may occur, and rarely, skin rash, urticaria, pruritus, and flushing. One case of thrombocytopenia has been reported in a patient with a history of conjunctival hemorrhages. Subjective complaints have been: dryness of throat, burning on swallowing, heartburn, sore throat, dizziness, and headache.

Usual Dosage: 3 Gm. (6 tablets) at night after a light supper.

Supplied: Tablets of 500 mg., envelopes of 6 tablets, boxes of 5 and 25 envelopes; also bottles of 500.

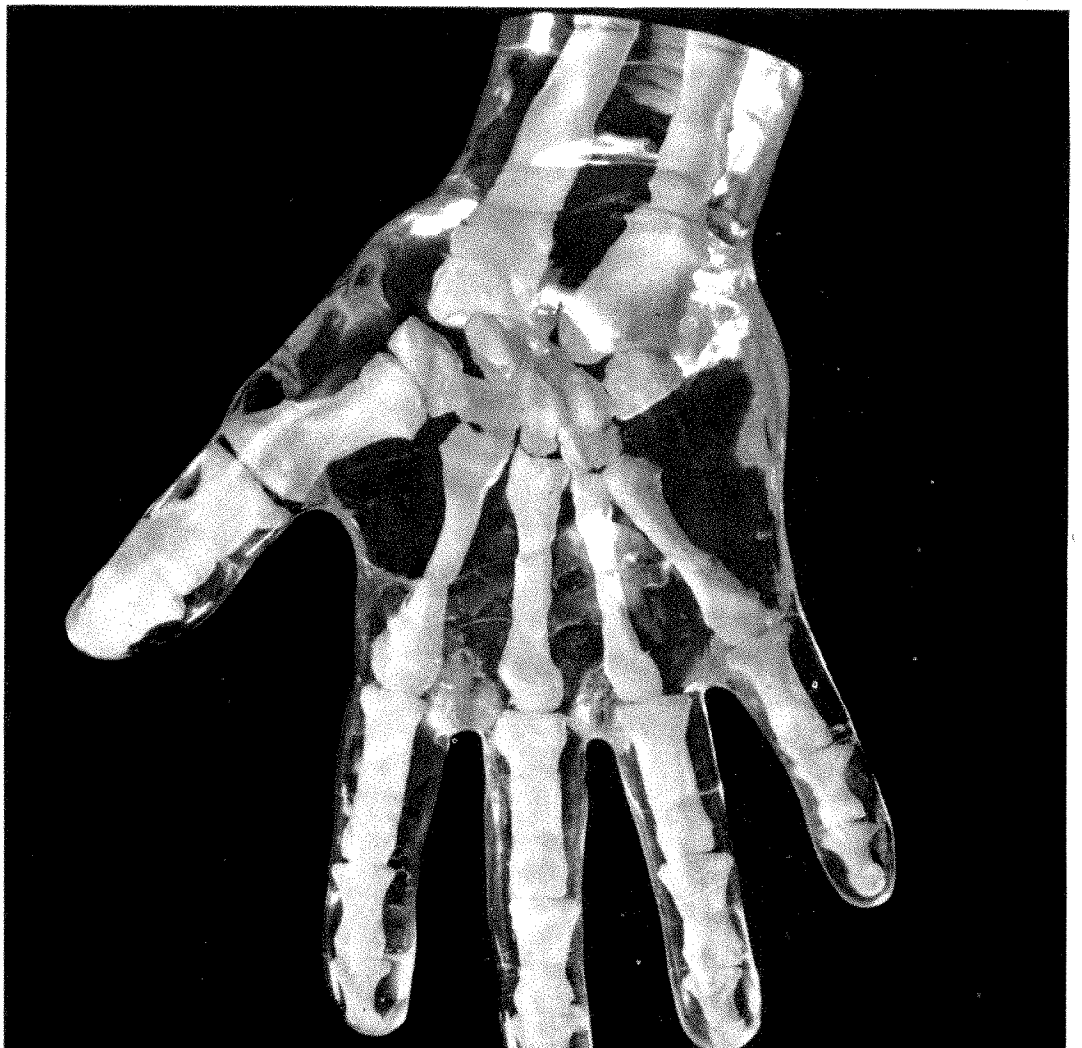
*Baker, H. L., Jr., and Hodgson, J. R. (Mayo Clinic and Mayo Foundation): Further studies on the accuracy of oral cholecystography, *Radiology 74*:239, Feb., 1960.

Telepaque® **in oral cholecystography and cholangiography provides the accurate picture with excellent tolerance**

brand of **iopanoic acid**

Winthrop **PIONEERS IN PRODUCTS FOR RADIOLOGIC DIAGNOSIS**

WINTHROP LABORATORIES
NEW YORK, N.Y. 10016



We can't give you a helping hand, but we'll sell you one.

3M X-Ray Phantoms help you in...

1. All studies normally requiring exposure to humans.
2. Teaching skeletal anatomy and its relation to surface marks.
3. Demonstrating preferred radiographic positions.
4. Demonstrating and measuring density, detail, distortion and contrast.
5. Determining optimum-exposure techniques—especially Cineradiographic, Planographic.
6. Photofluorographic, Mammographic and Seriographic.
7. Testing X-Ray apparatus including grinds, films, screen, etc.

Pictured is just one of our ten 3M X-Ray Phantoms. The other nine include: Skull, Dental, Pelvis, Foot and Ankle, Elbow, Knee, Chest, Breast and a 24x22cm. tissue-equivalent Step Wedge for comparative studies.

All 3M X-Ray Phantoms are adult human bones embedded in transparent, nongranular plastic. Specific gravity, atomic number, absorption and secondary radiation-emitting characteristics are virtually identical with living tissues.

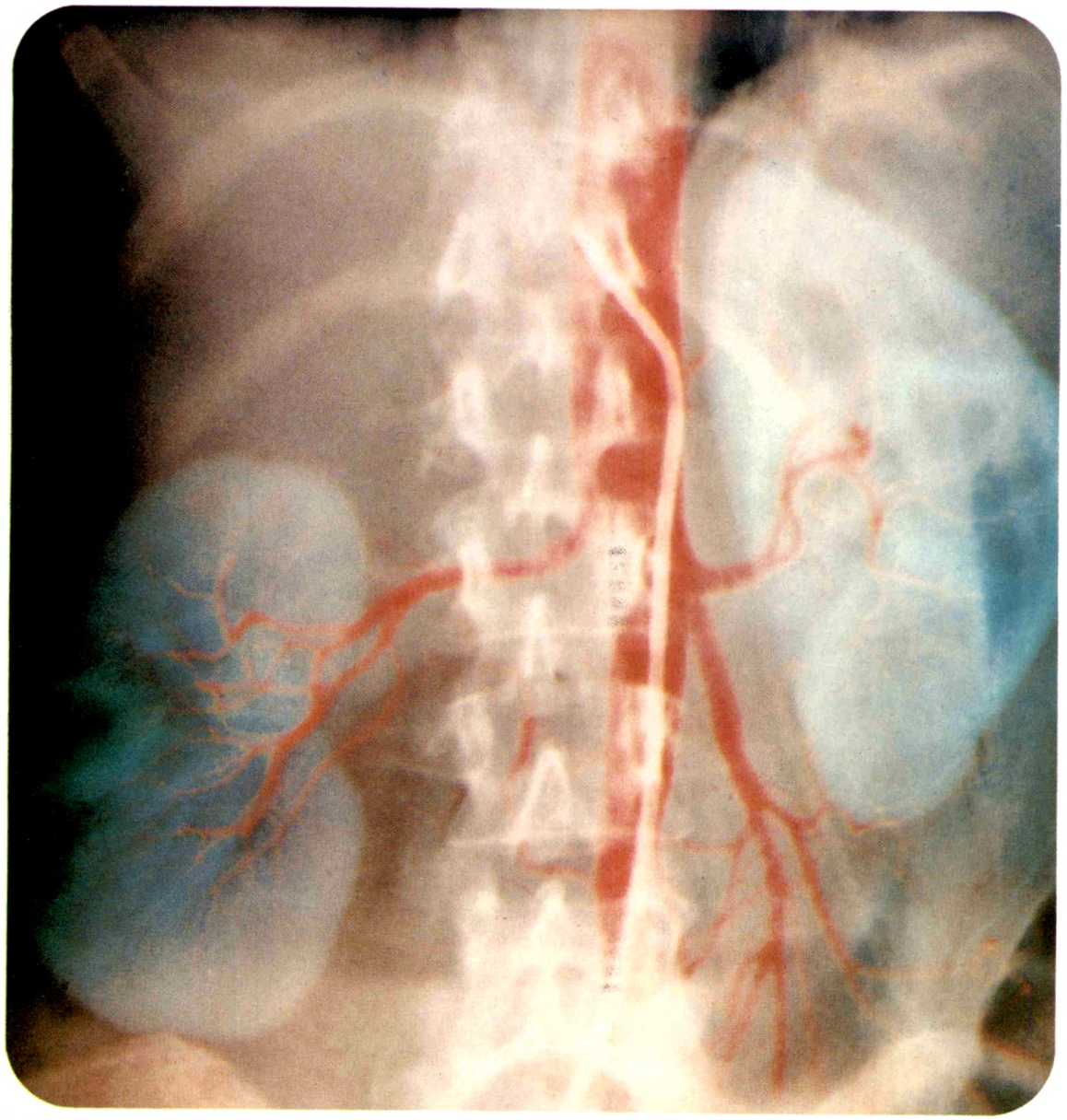
3M Phantoms are available from your X-Ray products dealer. For more information, contact him or write us directly.

Photographic Products 3M COMPANY

3M CENTER ST. PAUL MINNESOTA 55101

Aortography

(percutaneous retrograde catheter technique) using Hypaque® sodium 50% as the contrast medium



The six color films illustrated, in which Hypaque was used as contrast medium, were supplied through the courtesy of Robert E. Wise, M.D. of the Lahey Clinic Foundation and New England Baptist Hospital, Boston, Mass. The technique, employing ordinary x-rays, is described in the Lahey Clinic Foundation Bulletin *14*:131, 1965.

and you'll get the same precise black-and-white definition using

Hypaque® 50%

sodium

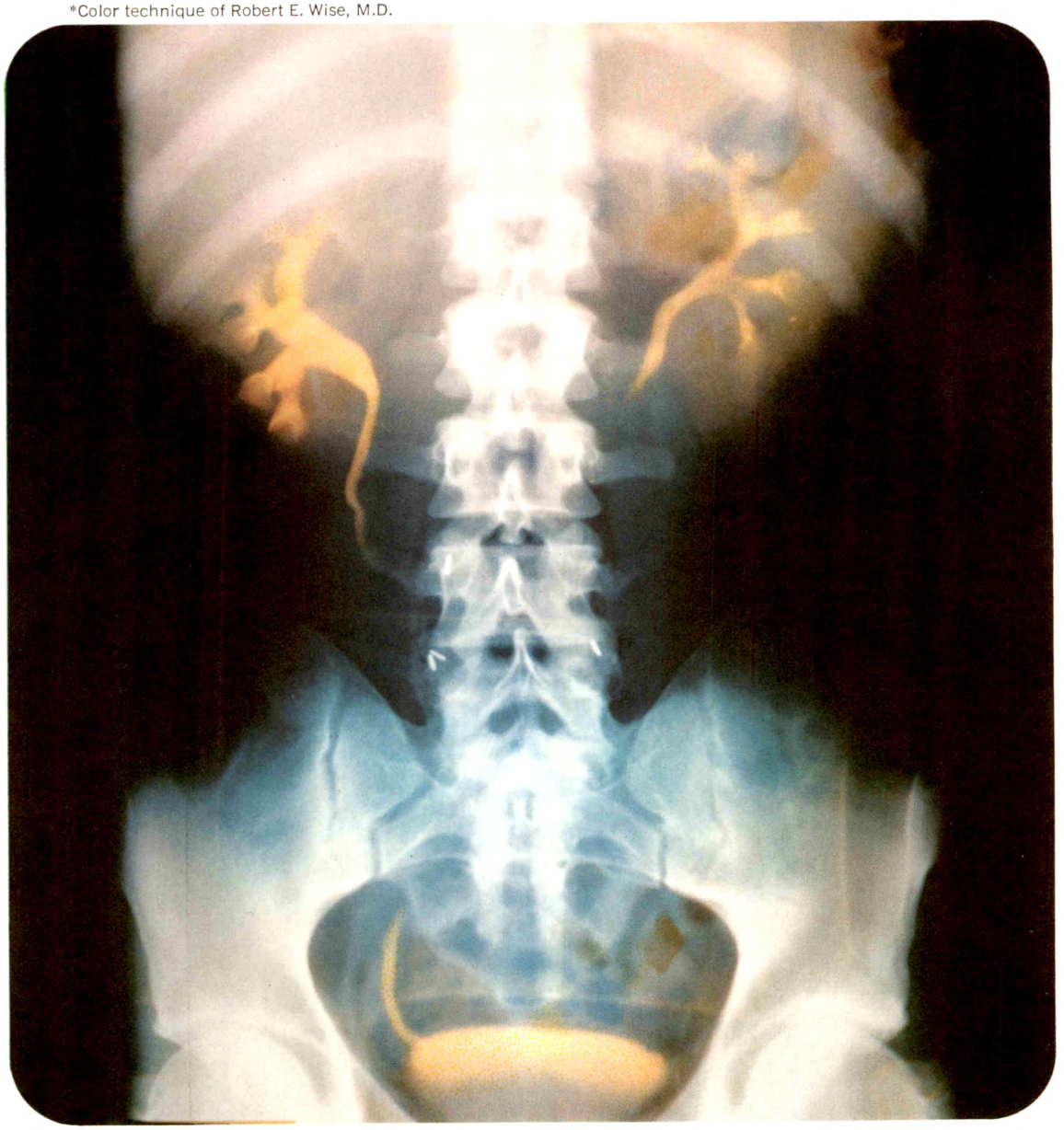
brand of **sodium diatrizoate**

Aortography with Hypaque sodium 50% may give valuable evidence in cases of renal agenesis, duplications or ectopia, or of polycystic kidney. Aortograms are also of importance in helping to demonstrate aneurysmal change or the degree of patency of the arteriosclerotic vessel, and in aiding the surgeon to determine proper surgical management if such is needed especially where a stenotic vessel is responsible for life-threatening renal hypertension. Aortograms with Hypaque 50% have provided clearly defined needed evidence of pathology prior to surgical intervention.

Excretory Urography

using Hypaque® sodium 50% as the contrast medium*

*Color technique of Robert E. Wise, M.D.



and you'll get the same precise black-and-white definition using

Hypaque® 50%
sodium

brand of **sodium diatrizoate**

Excretory urography with Hypaque sodium 50% provides the detection of urinary tract lesions, without interference with functional activity, without age limit and without anesthesia—important advantages when instrumentation is undesirable.

Cerebral Arteriography

using Hypaque® sodium 50% as the contrast medium*

*Color technique of Robert E. Wise, M.D.



and you'll get the same precise black-and-white definition using

Hypaque® 50%

sodium

brand of **sodium diatrizoate**

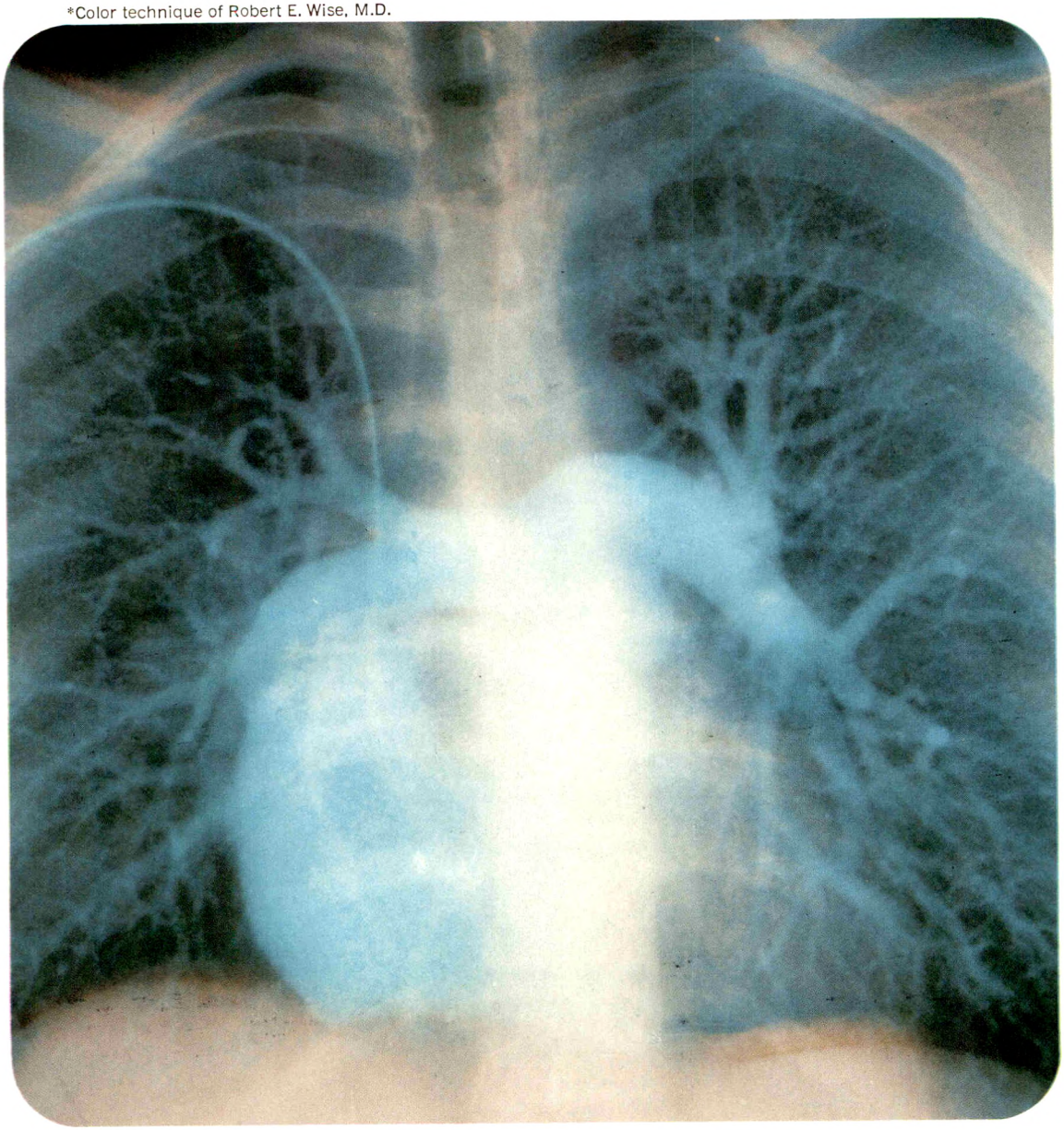
Cerebral arteriography with Hypaque sodium 50% has proved most useful in localizing and identifying intracranial lesions. Because it demonstrates both pathologic anatomy and physiology in such disorders as aneurysms, hematomas, angiomatous formations, meningiomas, glioblastoma multiforme, and other neoplasms, this procedure may provide diagnostic information frequently unobtainable by other means.

Please read the summary of prescribing information on the last pages of this unit

Angiocardiography

using Hypaque®-M, 75% as the contrast medium*

*Color technique of Robert E. Wise, M.D.



and you'll get the same precise black-and-white definition using

Hypaque®-M, 75%

brand of **sodium and meglumine diatrizoates**

Because the cardiac chambers and great blood vessels of the thorax can be effectively visualized with Hypaque-M 75% (90% may be used alternatively), it provides an invaluable aid in the diagnosis of a variety of congenital and acquired cardiac defects. Angiocardiography has also proved useful in the study of neoplastic and infectious diseases of the heart. Hypaque-M 75% used for this purpose is freely miscible with blood, relatively non-irritating and nontoxic in recommended dosage, and is rapidly eliminated by the kidneys.

Nephrotomography

using Hypaque®M, 90% as the contrast medium*

*Color technique of Robert E. Wise, M.D.



and you'll get the same precise black-and-white definition using

Hypaque®M, 90%

brand of **sodium and meglumine diatrizoates**

One of the newer methods employed to reveal the nature of renal lesions is nephrotomography —a combination of rapid intravenous nephrography and body-section radiography which provides precise delineation of renal parenchyma. Nephrotomography with Hypaque-M 90% is used primarily to differentiate renal cysts from neoplasms, but may also be indicated to distinguish renal from extrarenal masses and to demonstrate congenital anomalies of the kidney.

Please read the summary of prescribing information on the last pages of this unit

Retrograde Pyelography

using Hypaque® sodium 20% as the contrast medium*

*Color technique of Robert E. Wise, M.D.



and you'll get the same precise black-and-white definition using

Hypaque® 20%
sodium
brand of **sodium diatrizoate**

When loss of renal function or other causes result in unsatisfactory delineation of the urinary tract with intravenous techniques, retrograde pyelography with Hypaque sodium 20% solution can provide excellent anatomical details.

Please read the summary of prescribing information on the last pages of this unit.

Unsurpassed
• CONTRAST
• TOLERANCE

Pathology precisely defined
with

Hypaque® sodium 50% and 20%

brand of **sodium diatrizoate**

50%, ampuls of 30 ml., vials of 20, 30 and 50 ml.
20%, bottles of 100 ml.

or with

Hypaque®-M, 75% and 90%

brand of **sodium and meglumine diatrizoates**

75%, vials of 20 and 50 ml.
90%, vials of 20 and 50 ml.

Winthrop PIONEERS IN PRODUCTS FOR RADIOLOGIC DIAGNOSIS

WINTHROP LABORATORI
NEW YORK, N. Y. 10016

Summary of Full Prescribing Information

Hypaque® Sodium 50%

brand of **sodium diatrizoate, USP**

Sterile Aqueous Injection (Weight/Volume)

Excretory Urography and Drip Infusion Pyelography

Description: Hypaque sodium is sodium 3,5-diacetamido-2,4,6-triiodobenzoate, a radiopaque medium used to delineate internal structures.

Warning: Do not use Hypaque sodium for myelography. Injection of even a small amount into the subarachnoid space may produce convulsions and result in fatality.

General and Specific Precautions: Caution is advised in patients with a history of bronchial asthma, other allergic manifestations, or of sensitivity to iodine; these conditions represent a special risk, though not an absolute contraindication. To avoid or minimize possible allergic reactions, premedication with antihistamines may be considered. Benadryl (diphenhydramine hydrochloride) in the same syringe with Hypaque may result in precipitation. A test dose of contrast medium is not entirely reliable. Severe reactions, including fatalities, have occurred with a test dose as well as with the full diagnostic dose.

Caution is advised in patients with severe cardiovascular disease. In patients with impaired renal function and cardiovascular disease, drip infusion pyelography imposes a sudden osmotic and sodium load which can precipitate congestive heart failure. Contrast media injected into arteries or veins can promote sickling of red cells in susceptible individuals. In patients with reduced renal function, repeat of excretory or retrograde pyelography should be delayed at least 48 hours to avoid temporary suppression of urine. In preparation for excretory urography of patients with multiple myeloma, partial dehydration is not recommended, since this may predispose to the precipitation of myeloma protein in the kidney tubules. When thyroid function studies (PBI and 24-hour radioiodine uptake levels) are indicated, they should be performed *prior* to radiographic studies or several days afterwards, to avoid inaccurate results.

Hypaque sodium 50% should always be injected at body temperature.

General and Specific Adverse Reactions: Adverse reactions, usually of a minor nature, have occurred in 10-14 per cent of patients who have received Hypaque intravenously. Reactions due to *faulty technique* include hematomas and ecchymoses, following extravasation from the vein, and pyrogenic reactions. *Hemodynamic reactions* include vasodilatation with flushing, hypotension and, rarely, vein cramp or thrombophlebitis. Serious *cardiovascular reactions* include rare cases of cardiac arrhythmias (e.g., ventricular fibrillation), shock, and cardiac arrest. Transient proteinuria may occur occasionally following the injection of radiopaques and, rarely, oliguria and anuria have been reported secondary to a hypotensive reaction. *Allergic reactions* include asthmatic attacks, nasal and conjunctival symptoms, cutaneous reactions such as urticaria and, rarely, anaphylactic shock, sometimes with fatal outcome. Severe reactions may also be manifested by signs and symptoms relating to the *respiratory system* (dyspnea, cyanosis, pulmonary or laryngeal edema), or to the *nervous system* (restlessness, confusion, or convulsions). *Other reactions* include nausea, vomiting, excessive salivation, anxiety, headache, and dizziness. Infrequently, "iodism" (salivary gland swelling) from organic compounds appears two days after exposure and subsides by the sixth day. Reactions to drip infusion pyelography may not appear until some hours after the examination.

Angiography

(Peripheral Arteriography and Venography)

Precautions (See also General Precautions): Extreme caution is advised in considering peripheral arteriography in patients suspected of having thromboangiitis obliterans (Buerger's disease). Any procedure (even needling or insertion of a catheter) may induce a severe arterial and/or venous spasm. Caution is also advisable in patients with severe ischemia associated with ascending infection.

Adverse Reactions (See also General Adverse Reactions): In addition to those listed under General Adverse Reactions, are those due to arterial trauma during the procedure (i.e., needling, insertion of catheter, subintimal injection, perforation, etc.) as well as to the hypertonicity or effect of the medium; also reported are transient arterial spasm, extravasation, hemorrhage, hematoma with tamponade, injury to nerves proximal to artery, thrombosis (rare in venography; if vein is irrigated following injection), dissecting aneurysm, arteriovenous fistula, (e.g., with accidental perforation of femoral artery and vein during needling), transient leg pain from contraction of calf muscles in femoral arteriography; transient hypotension after intraarterial (brachial) injection, and brachial plexus injury with axillary artery injections.

Cerebral Angiography: Because of the special techniques required, it is recommended that Hypaque sodium be used for this purpose only by persons skilled and experienced in carrying out this procedure.

Contraindication: Carotid angiography should be avoided during the progressive period of a stroke, since this increases the risk of cerebral complications.

Precautions (See also General Precautions): Select patients for this procedure with care. Use the 50 per cent solution with caution in extreme senility (but not old age, *per se*); advanced arteriosclerosis; severe hypertension; and cardiac decompensation.

The diagnostic value of the procedure, according to many authorities, when employed early enough in locating lesions amenable to surgery, may outweigh the added risk to patients who have recently experienced cerebral embolism or thrombosis (stroke syndrome). A small number of postangiographic fatalities, including progressive thrombosis, have occurred in which the procedure did not appear to play a role.

Patients with severe cerebrovascular disease may be examined primarily by indirect methods of angiography.

Care should be exercised to avoid contaminating catheters, syringes, needles, and contrast media with glove powder or cotton fibers.

Angiography is hazardous in subarachnoid hemorrhage. In migraine, the procedure can be hazardous because of ischemic complications, particularly if performed during or soon after an attack.

Adverse Reactions (See also General Adverse Reactions): The major sources of complications are faulty technique, occlusive atherosclerotic vascular disease, repeated injections of the contrast media, and higher doses than those recommended.

Untoward reactions are mostly mild and transient, although permanent visual field defects and deaths have been reported.

Vascular reactions: flushing, vessel spasm, thrombophlebitis, and cutaneous petechiae.

Neurologic complications: transient cerebral blindness, neuromuscular disorders, convulsions, coma, hemiparesis, unilateral dysesthesias, visual field defects, aphasia, and respiratory difficulties.

Aortography

Precautions (See also General Precautions): Special caution is advised to avoid inadvertent intrathecal injection when using the translumbar technique. The incidence and severity of reactions or complications that may occur are influenced by: the care and experience with which the procedure is performed; the amount and type of medium used; the age and condition of the patient; and the premedication and anesthesia used. Since aortography is not without some danger, it should be performed only by those experienced in the technique. Wherever possible, repeated injections of the solution during a single study should be avoided.

Adverse Reactions (See also General Adverse Reactions): Renal damage and shutdown; neurologic complications such as transverse myelitis or paraplegia; cardiovascular complications such as shock, cardiac arrest or failure, coronary occlusion, arterial thrombosis, embolism, and perforation of vessels; extravasation or hemorrhage from the puncture site or retroperitoneal catheter perforation; necrosis of the intestinal wall; acute pancreatitis; deaths; diffuse cutaneous petechiae; subintimal injection and aortic dissection.

Intraosseus Venography (See General Precautions and Adverse Reactions): A general anesthetic is sometimes necessary since the method is painful. Occasionally, extravasation of the contrast medium from the needle into the soft tissue may occur.

Direct Cholangiography

Precaution (See also General Precautions): This procedure should be used with caution in the presence of acute pancreatitis, injecting no more than 5 to 10 ml. without undue pressure.

Adverse Reactions (See also General Adverse Reactions): These may be attributed to injection pressure or excessive volume of the medium, resulting in overdistention. Such pressure may produce a sensation of epigastric fullness, followed by moderate pain in the back or right upper abdominal quadrant, which will subside when injection is stopped.

Some of the medium may enter the pancreatic duct and cause a transient serum amylase elevation 6 to 18 hours later, without apparent ill effects. Pancholangitis resulting in liver abscess has been reported. Occasionally, nausea, vomiting, fever, and tachycardia have been observed.

Hysterosalpingography

Contraindications: Menstruation, active or imminent; infection in any part of the genital tract, including the external genitalia; pregnancy, known or suspected. Use not advised for six months after end of pregnancy, or 30 days after conization or curettement.

Precaution (See also General Precautions): Caution should be exercised in patients with known or suspected carcinoma to avoid possible spread of the lesion by the procedure.

Splenoportography

Precautions (See also General Precautions): Procedure should be performed with caution on patients with blood dyscrasias, a tendency to severe bleeding, or a spleen recently become tender and palpable.
Adverse Reactions (See also General Adverse Reactions): Persistent hemorrhage with hemoperitoneum has been reported, and, in some instances, hemorrhage has required splenectomy.
How Supplied: Ampuls of 30 ml., boxes of 1, 10, and 25. A 1 ml. sensitivity test ampul is furnished with each ampul. Vials of 20 and 30 ml., rubber stoppered, boxes of 1, 10, and 25. Vials of 50 ml., rubber stoppered, boxes of 1 and 10. Each vial contains sufficient excess to permit withdrawal of 1 ml. for testing sensitivity.

If the solution is chilled, crystals may form but will readily dissolve if the ampul or vial is placed in moderately hot water before use. Cool to body temperature before injecting.

Hypaque® Sodium 20%

brand of **sodium diatrizoate**

Sterile Aqueous Solution 20% (weight/volume)

Precautions: It has long been known that oliguria or anuria may rarely follow bilateral retrograde pyelography or uncomplicated cystoscopic ureteral manipulation. Various mechanisms have been proposed to explain this occurrence, such as reflex anuria, edema, and occlusion of the ureteral orifices from local trauma, pressure, manipulation, sensitivity to the radiopaque medium or to residual disinfecting antiseptic on ureteral catheters, pyelotubular backflow, transient interstitial renal edema with increased pressure, and reduced renal blood flow. Because of the possibility of acute renal failure following bilateral retrograde pyelography, some authors conclude that retrograde pyelography should be done on only one side at a time.
Side Effects: The nonirritating properties of the medium minimize the likelihood of ureteropelvic spasm; in addition, a more natural outline of the upper urinary tract is obtained because of these properties. There is also a decrease in the incidence and severity of discomfort and colic following retrograde examination. Excellent tolerance was evidenced by notably few untoward reactions. Minor side reactions, which occurred in a few patients, consisted of nausea, vomiting, excessive salivation, and sweating. There was no indication of irritation of the urinary tract mucosa that could be attributed to the medium.

With Hypaque Sodium 20 per cent, reflux into the blood stream or lymphatics (pyelovenous or pyelolymphatic backflow) as a result of undue pressure of administration is not apt to result in a generalized reaction, since intravenous injection of more than double this concentration has been well tolerated.

Hypaque® M, 75%

brand of **sodium and meglumine diatrizoates**

Sterile Aqueous Injection 75% (weight/volume)

Caution: The 75 per cent concentration is intended primarily for angiocardiography, nephrotomography and selected cases of peripheral angiography. Hypaque sodium (brand of diatrizoate sodium) 50 per cent solution is recommended for excretory urography, cerebral angiography and most cases of peripheral angiography.
Warning: Do not use Hypaque-M, 75 per cent for myelography. Injection of even a small amount into the subarachnoid space may produce convulsions and result in fatality.

Angiocardiography

Contraindications: Use of Hypaque-M, 75 per cent is contraindicated in patients with advanced renal destruction associated with severe uremia. Hypaque-M 75 per cent should not be used for myelography.
Precautions: 1. Caution is advised in patients with hyperthyroidism, hypertension, active tuberculosis and a history of allergy, especially to iodine. Angiocardiography and nephrotomography should be performed cautiously in patients with heart disease and circulatory failure and should not be employed in patients who are in collapse or who are critically ill or debilitated. A renal function test is advisable before administration of the 75 per cent solution.

2. Prior to the examination, the patient may be tested for sensitivity to the radiopaque medium. (See Side Effects and Sensitivity Tests.) Patients who show an idiosyncrasy should not be given the drug.

3. Premedication with a barbiturate is advisable if the patient is extremely nervous. Demerol (brand of meperidine), chlor-

promazine and antihistamines have also been recommended for premedication. Such antihistamines as chlorpheniramine maleate or tripelennamine hydrochloride may be administered about 30 minutes before injection of the radiopaque medium or may be combined with it in a single injection. Many authorities recommend general anesthesia for small children and uncooperative patients.

4. Facilities for resuscitation including a mask with a breathing bag and pure oxygen should be available for immediate administration in case of severe reaction.

5. The sensations to be experienced should be described to the patient in order to allay apprehension before injection and to prevent excitement afterward.

6. To facilitate venipuncture, the needle should be sharp, the arm extended and the vein large and fully distended.

7. The syringe must be scrupulously clean in order to prevent sticking of the plunger during injection.

8. If crystals form, the solution should be warmed and agitated until they have redissolved. Injection should be made only when the solution is clear and is at a temperature of approximately 37.5° C.

9. Injection should be made only when there is free communication between needle and vein. When in doubt, another vein should be tried or the test postponed. Vein and needle should be watched during injection to prevent displacement of the needle or overdistention of the vein. If extravasation occurs, the injection should be stopped and a quantity of physiologic saline solution administered through the needle to dilute the radiopaque medium and to lessen the possibility of irritation.

10. Some authorities advise that repeated injections should not be given in close sequence and, if possible, should be avoided.

Side Effects and Sensitivity Tests: As with other radiopaque mediums, certain side effects occasionally may be encountered, although the 75 per cent solution has been well tolerated when given in recommended dosages. Serious complications following angiocardiography may be due to varying and perhaps unrelated factors. Symptoms may be due to the speed of injection and the anxiety and psychic stress associated with the examination, as well as to the material injected. Side effects will usually be minor and transient and may include a sensation of warmth and flushing, nausea, vein cramp, mild tachycardia, metallic or acid taste, tightness in the chest, headache, cough or urticaria. Delayed reactions may occur. Venous thrombosis has not been observed in patients receiving the 75 per cent solution, but as with any rapidly injected hypertonic solution, the possibility of this complication exists.

Angiocardiographic contrast mediums may produce symptoms of an anaphylactic nature in sensitive persons. Patients should be observed carefully during injection, as serious reactions including fatalities have occurred with most mediums. Since it is believed that reactions to intravenously administered organic iodine radiopaque agents are more likely to develop in patients with allergic diathesis, special care is advisable in persons with a history of asthma or other allergic manifestations.

Various methods have been advocated to detect sensitivity to contrast mediums, particularly conjunctival, oral, intradermal and intravenous testing. Conjunctival, oral and intradermal tests are not reliable, since reactions to them are generally caused by direct local vascular effect. Occasionally a severe reaction in the eye has followed a conjunctival test. An intravenous test is more likely to demonstrate sensitivity, although a negative reaction does not necessarily rule out the possibility. A small dose of 0.5 to 1 ml. is slowly injected intravenously over a period of one minute, followed by a period of observation sufficiently long to detect delayed reactions. Although allergic reactions generally occur quickly, occasionally they may not be manifested for 10 or even 15 minutes.

Warning signs and symptoms of possible intolerance or allergy include respiratory difficulty (wheezing, dyspnea or sensation of suffocation or tightness in the throat or chest), sneezing, itching, urticaria, nausea or vomiting and fainting.
Treatment of Reactions: (Same as with Hypaque Sodium 50%)

Nephrotomography

Contraindications, Precautions, Side Effects and Treatment of Reactions: See Angiocardiography.

Hypaque® M, 90%

brand of **sodium and meglumine diatrizoates**

Sterile Aqueous Injection 90% (weight/volume)

Caution: Hypaque-M, 90 per cent is intended primarily for angiocardiography, nephrotomography, hysterosalpingography and selected cases of peripheral angiography. Hypaque sodium

Hypaque®-M, 90%
brand of **sodium and meglumine diatrizoates (cont.)**

50 per cent solution is recommended for excretory urography, cerebral angiography and most cases of peripheral angiography. *Warning:* Do not use Hypaque-M, 90 per cent for myelography. Injection of even a small amount into the subarachnoid space may produce convulsions and result in fatality.

Angiocardiography

Contraindications: Use of Hypaque-M, 90 per cent is contraindicated in patients with advanced renal destruction associated with severe uremia. Hypaque-M, 90 per cent should not be used for myelography.

Precautions: 1. Caution is advised in patients with hyperthyroidism, hypertension, active tuberculosis and a history of allergy, especially to iodine. Angiocardiography and nephrotomography should be performed cautiously in patients with heart disease and circulatory failure and should not be employed in patients who are in collapse or who are critically ill or debilitated. A renal function test is advisable before administration of Hypaque-M, 90 per cent.

2. Prior to the examination, the patient may be tested for sensitivity to Hypaque-M, 90 per cent. (See Side Effects and Sensitivity Tests.) Patients who show an idiosyncrasy to Hypaque-M, 90 per cent should not be given the drug.

3. Premedication with a barbiturate is advisable if the patient is extremely nervous. Demerol (brand of meperidine), chlorpromazine and antihistamines have also been recommended for premedication. Such antihistamines as chlorpheniramine maleate or tripelennamine hydrochloride may be administered about thirty minutes before injection of Hypaque-M, 90 per cent or may be combined with it in a single injection. Many authorities recommend general anesthesia for small children and uncooperative patients.

4. Facilities for resuscitation including a mask with a breathing bag and pure oxygen should be available for immediate administration in case of severe reaction.

5. The sensations to be experienced should be described to the patient in order to allay apprehension before injection and to prevent excitement afterward.

6. To facilitate venipuncture, the needle should be sharp, the arm extended and the vein large and fully distended.

7. The syringe must be scrupulously clean in order to prevent sticking of the plunger during injection.

8. Hypaque-M, 90 per cent should be warmed and agitated until all suspended crystals have redissolved. Injection should be made only when the solution is clear and is at a temperature of approximately 37.5°C.

9. Injection should be made only when there is free communication between needle and vein. When in doubt, another vein should be tried or the test postponed. Vein and needle should be watched during injection to prevent displacement of the needle or overdistention of the vein. If extravasation occurs, the injection should be stopped and a quantity of physiologic saline solution administered through the needle to dilute the Hypaque-M, 90 per cent and to lessen the possibility of irritation.

10. Some authorities advise that repeated injections should not be given in close sequence and, if possible, should be avoided.

Hypaque®-M, 90%
brand of **sodium and meglumine diatrizoates (cont.)**

Side Effects and Sensitivity Tests: Serious complications following angiocardiography may be due to varying and perhaps unrelated factors. Symptoms may be due to the speed of injection and the anxiety and psychic stress associated with the examination, as well as to the material injected. Side effects noted with Hypaque-M, 90 per cent were usually of a minor and transient nature and included a sensation of flushing or warmth, nausea, vein cramp, mild tachycardia, metallic or acid taste, tightness in the chest, headache, cough or urticaria. Delayed reactions may occur. Venous thrombosis has been observed in patients following the percutaneous insertion of the injection needle. This complication may be anticipated, however, when concentrated hypertonic solutions are injected rapidly. In skilled hands, the administration of Hypaque-M, 90 per cent is attended by comparatively few untoward reactions.

Angiocardiographic contrast mediums may produce symptoms of an anaphylactic nature in sensitive persons. Patients should be observed carefully during injection, as serious reactions including fatalities have occurred with most mediums. Since it is believed that reactions to intravenously administered organic iodine radiopaque agents are more likely to develop in patients with allergic diathesis, special care is advisable in persons with a history of asthma or other allergic manifestations.

Various methods have been advocated to detect sensitivity to contrast mediums, particularly conjunctival, oral, intradermal and intravenous testing. Conjunctival, oral and intradermal tests are not reliable, since reactions to them are generally caused by a direct local vascular effect. Occasionally a severe reaction in the eye has followed a conjunctival test. An intravenous test is more likely to demonstrate sensitivity, although a negative reaction does not necessarily rule out the possibility. A small dose of from 0.5 to 1 ml. is slowly injected intravenously over a period of one minute, followed by a period of observation sufficiently long to detect delayed reactions. Although allergic reactions generally occur quickly, occasionally they may not be manifested for ten or even fifteen minutes.

Warning signs and symptoms of possible intolerance or allergy include respiratory difficulty (wheezing, dyspnea or sensation of suffocation or tightness in the throat or chest), sneezing, itching, urticaria, nausea or vomiting and fainting. *Treatment of Reactions:* (Same as with Hypaque Sodium 50%)

Nephrotomography

Contraindications, Precautions, Side Effects and Treatment of Reactions: See Angiocardiography.

Hysterosalpingography

Contraindications: The procedure should not be performed during the menstrual period or when menstrual flow is imminent, nor should it be performed when infection is present in any portion of the genital tract, including the external genitalia. The procedure is also contraindicated for pregnant women or for those in whom pregnancy is suspected. Its use is not advised for six months after termination of pregnancy, or for thirty days after conization or curettement.

Precautions: In patients with carcinoma or in those in whom the condition is suspected, caution should be exercised to avoid possible spread of the lesion by the procedure.

For more detailed information on these products, please read the package circulars.

Pathology Precisely Defined

Hypaque® Sodium 20% and 50%
brand of **sodium diatrizoate**

Hypaque®-M, 75% and 90%
brand of **sodium and meglumine diatrizoates**

Winthrop **PIONEERS IN PRODUCTS FOR RADIOLOGIC DIAGNOSIS**

PRINTED IN U.S.A. ISSUED JAN. 1969 (1326M)

SIEMENS

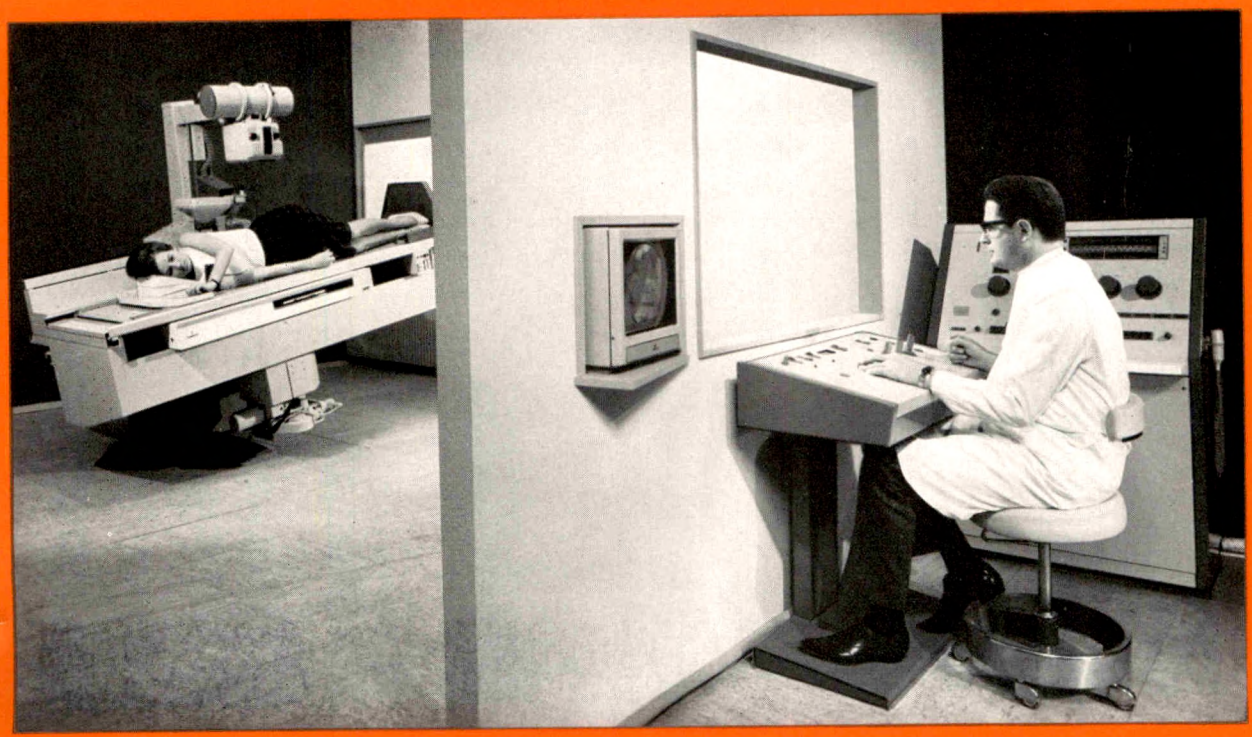
SIREGRAPH System Approach

From its remote control console to the smallest table accessory, the SIREGRAPH is the „System Approach" to the radiologists' most pressing problems – how to obtain the highest possible consistent quality of information and how to make the most efficient use of his time.

Outstanding features include:

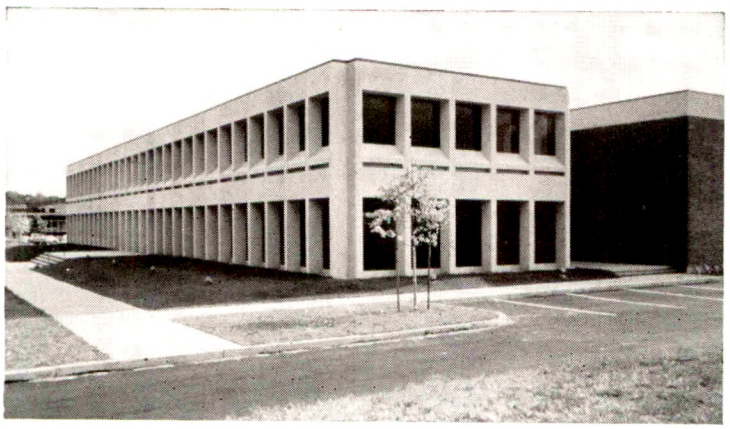
- 90/90 continuously variable speed motor driven tilting table
- Rotating cradle (optional)
- Two way power top
- Fully automatic undertable spot film device for use with five various cassette sizes
- Built-in 10/6 SIRECON Image Intensifier with television which tracks the X-ray beam through all angulations of X-ray tube or table
- Routine and special techniques including planigraphy and zonography
- Choice of recording methods from image system 70 – 35 mm or 16 mm cine

SIEMENS MEDICAL OF AMERICA INC.
685 LIBERTY AVENUE, UNION, N.J. 07083



This is the plant our customers built

Yes, when we outlined the specifications for our new premises in Paramus, N. J., foremost in our planning was our desire to provide our customers with the best possible service for the best possible products. We believe we have succeeded in this award-winning plant.



The new building shown at the left houses the Ilford executive and sales offices, the various darkrooms and demonstration rooms, and the national distribution center (in the rear) for Ilford products. The latter also supplies Ilford warehouses in Georgia and California.

BETTER DELIVERY SERVICE:
The new Ilford warehouse (below) contains 500,000 cubic feet of storage space and is equipped with the latest fork-lift equipment.

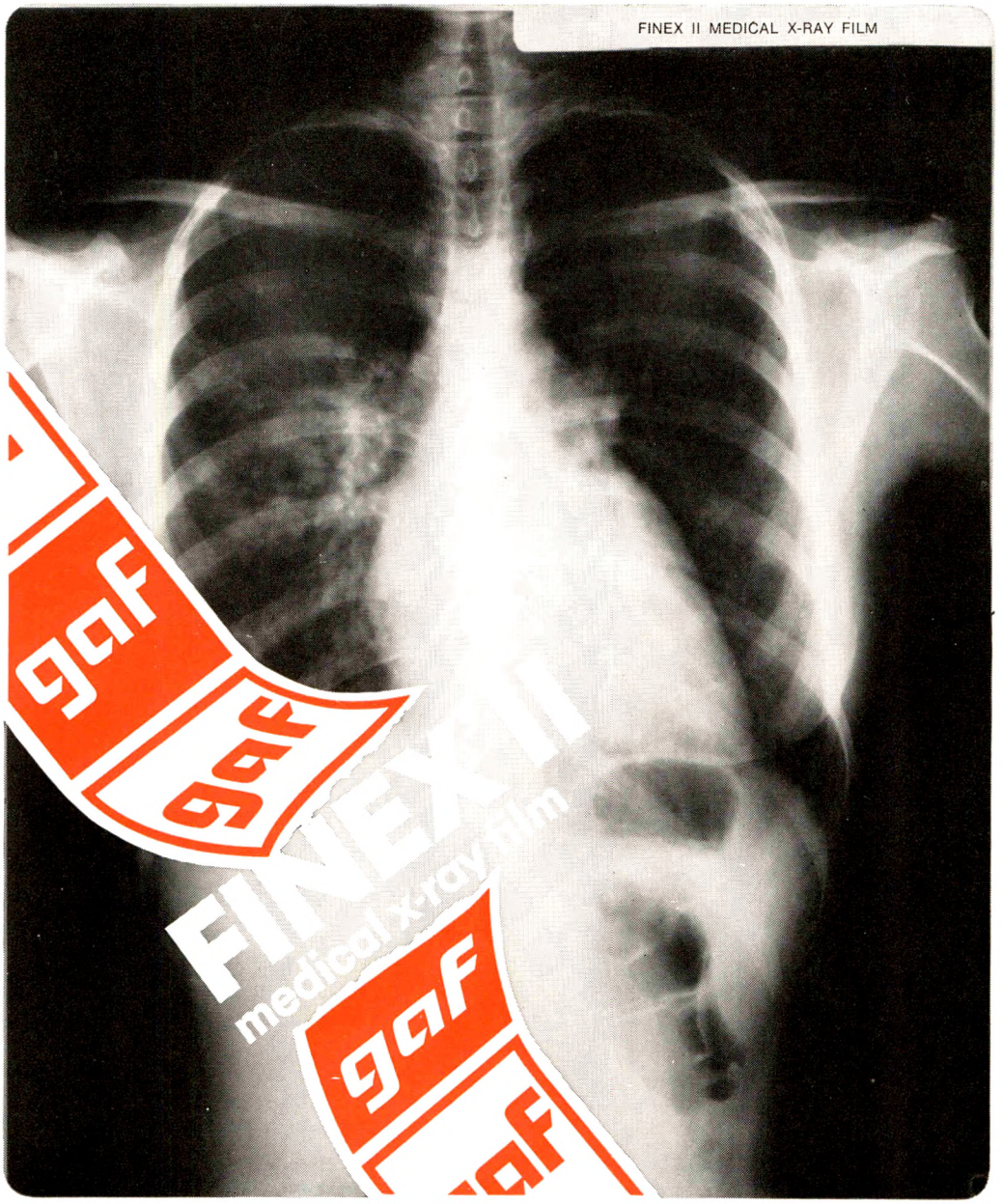


BETTER TECHNICAL SERVICE:
The Ilford film dark room (above) is one of several designed to provide top-notch technical information to Ilford customers.



ILFORD INC.

West 70 Century Road, P.O. Box 288, Paramus, N. J. 07652
1217 East El Segundo Boulevard, El Segundo, Calif. 90245
3566 Elm Street, Hapeville, Ga. 30054



Fine —
Finex™ II is an extra-fine grain film on a polyester base. Can be used in all processing systems, automatic and manual.

Finer —
Finex II gives a finer radiographic image, and dries better in marginal processing. No base fog.

FINEX II
A medium speed, 90 second film. Completely interchangeable. The perfect complement to GAF-X® film.

* Trademark of GAF Corporation

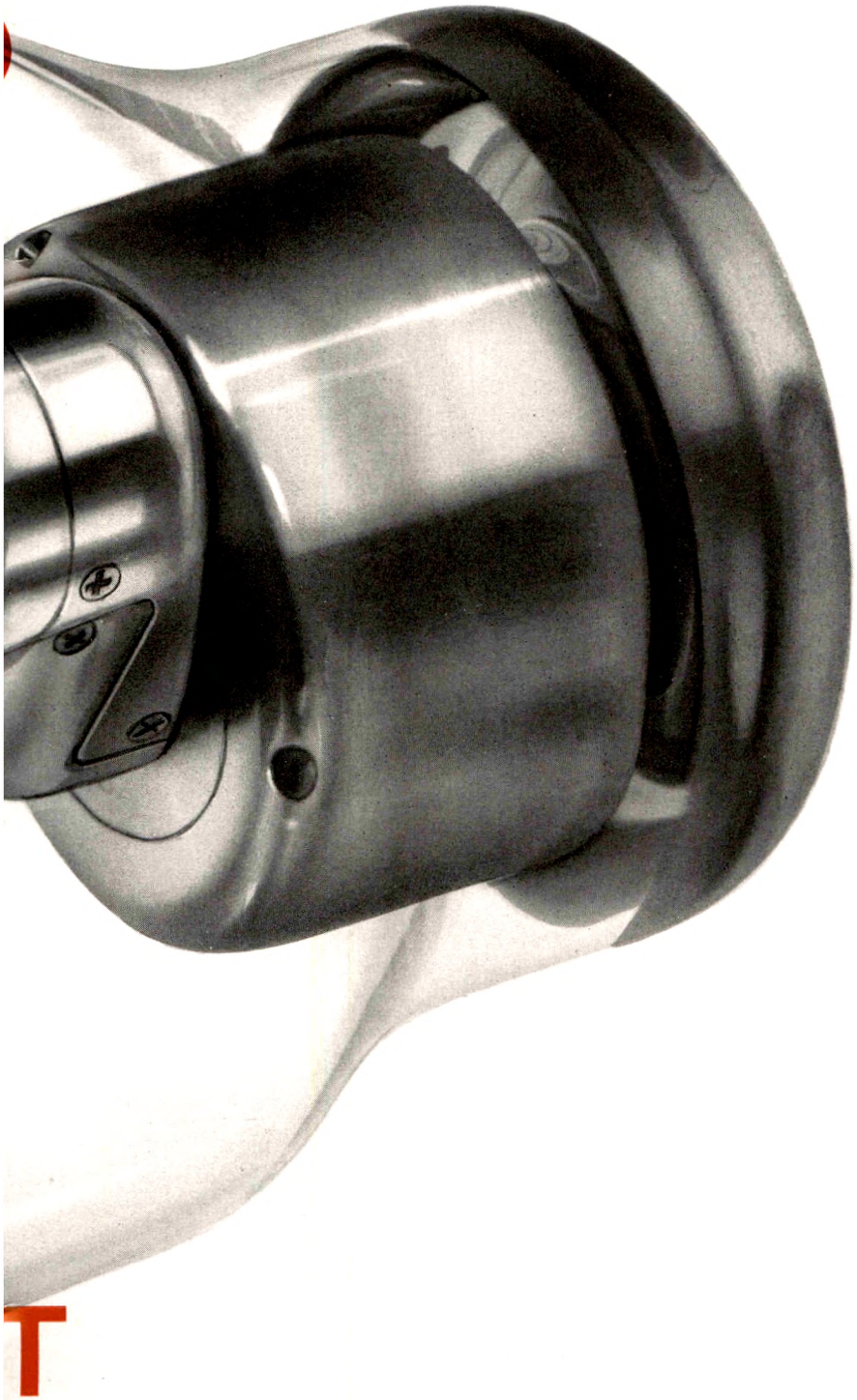
gaf

GAF Corporation
140 West 51 Street, New York, N.Y. 10020

A NEW LINE OF HEAVY ROTATING ANODE X-RAY THAT LAST AND LAST

AND LAST AND LAST AND LAST

DUTY TUBES



T

the remarkable new
DURATRONS
by **DUNLEE**

Designed to fit most housing

Today's X-ray department. More traffic. More sophisticated. More exposures per hour. Someone had to develop an X-ray tube insert to meet the demands of today's radiology.

Dunlee did.

Superbly engineered, the Dunlee Duratron 175 and 140 rotating anode tubes have a high heat storage capacity, 175,000 H.U. on the 175 and 140,000 H.U. on the 140. Their high dissipation rate makes them applicable for all types of fluoroscopic, spot film and general radiographic service.

Specially constructed targets (rhenium-tungsten-molybdenum on the Duratron 175, enlarged solid tungsten on the 140) assure a tube life unsurpassed in the industry.

Specify the X-ray tube insert designed for today's radiology. Duratron by Dunlee. As a new tube unit with its own Duratron housing or as a replacement tube in most housings.

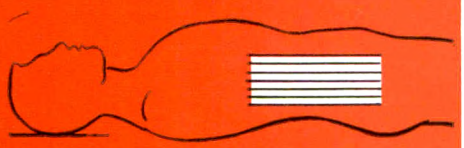
WARRANTY

Dunlee's Material and Workmanship Warranty is our expression of confidence and your assurance of the highest production and inspection standards.

Learn more about the benefits of the new Duratrons by Dunlee Ask your X-ray dealer or write.

DUNLEE CORPORATION
A PICKER CORPORATION SUBSIDIARY
1023 SOUTH CERNAN DRIVE
BELLWOOD, ILLINOIS 60104

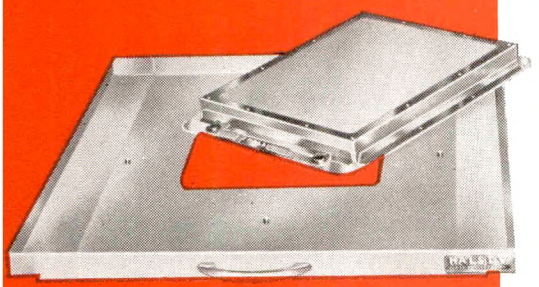
for body section radiography...



Halsey Multiple Film Cassettes

Multi-Sette Jr. "3-5"

3 or 5 films at a single exposure



Multi-Sette Jr. "3-5"

Utilizes a special book of matched screens of different speeds to provide comparable density and detail in each of the films.

The 3-film model has 1 cm spacing between adjacent films; the 5-film model, ½ cm spacing.

Fits the conventional Bucky without requiring modifications, by means of the special adapter tray supplied. Precision-built, with stainless steel frame, aluminum door and magnesium front. Opens and shuts easily.

Available in a full range of sizes with DuPont or Radelin screen book. The 3-film and 5-film books are interchangeable.

Multi-Sette "7"

7 films at a single exposure



Multi-Sette "7"

For use with open table only

Can be installed in the Bucky housing after a modification (which does not interfere with conventional use). Spacing between adjacent films is 1 cm.

Available in a full range of sizes, with DuPont or Radelin screen book.

Multi-Sette Plesiosette "4"

4 films at a single exposure



Multi-Sette Plesiosette "4"

For close-section radiography

Has the same outside dimensions as conventional cassettes, so no adapter tray or Bucky modification is required. Spacing between adjacent films is 1 mm.

Available in 8 x 10″ and 10 x 12″ sizes, with Radelin PLT screen book.

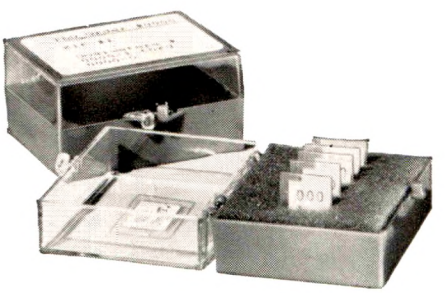
Write for detailed literature

HALSEY

HALSEY X-RAY PRODUCTS, INC.
1425-37th STREET, BROOKLYN, N.Y. 11218

CHICAGO: 7321 Monticello Avenue, Skokie, Illinois 60076
LOS ANGELES: 1816 W. 8th St., Los Angeles, Calif. 90057

TLD Custom Dosimeter Service, independently and individually calibrated, now available under professionally controlled standards.



Profit from the unique advantages of this individually calibrated LiF dosimeter for any dosage measurement in which the wide dosage range and large energy independence of these dosimeters offer an advantage. A simple-to-use service for measurement of depth dose, field distribution, and scores of other applications. Offers real exactitude in medical radiation control and testing in diagnostic and therapeutic procedures, or in industrial radiation control and testing. For more complete information on TLD Custom Dosimeter Service in the light of your needs, send full particulars concerning your requirements. No obligation, of course.

Check these advantages of TLD Custom Dosimeter Service against your requirements.

SPECIFICATIONS

Provided in sets of 5 solid state LiF dosimeters plus one control.

- Complete readout and reporting upon return to us.
- Exposure range 10^{-2} to 10^{5}R.
- Each dosimeter individually calibrated.
- Standard error less than 5% for exposures above 100 mr.
- Dose rate independent up to at least 2 x 10^{8}R per second.
- Energy response independent for X and Gamma radiations down to 100 KEV with less than 40% energy dependence for lower energies to 18 KEV.
- Dosimeters can be furnished sealed in sterile tubing.

^{6}LiF, ^{7}LiF, and CaF:Dy solid state dosimeters also available.

R.S. Landauer JR. & CO.
A Division of Technical Operations, Inc.
Landauer and Gardray Health And Safety Services
GLENWOOD SCIENCE PARK, GLENWOOD, ILLINOIS 60425 (312) 755-7000

The no-mix.

We took the construction work out of barium sulfate.

We premixed it into a smooth, creamy, instantly ready esophageal contrast medium.

Before, coating was often a hit-or-miss operation ('home-brewed' barium can be too thin, too thick or just plain settled out).

Not anymore.

Now, in seconds, you can photograph your patient's esophageal tract...easily take 3, 4, even 5, plates after an initial dose. In many patients the coating of Esophotrast lasts up to 15 minutes (ample time for fluoroscopy and radiography of the esophagus and evaluation of heart size).

Now you don't have to cajole your patients into drinking cupful after cupful of barium...the 1 oz. of Esophotrast, usually all that's needed, is nongritty and fruit-flavored–a really pleasant medium to take.

And it's just a squeeze of a tube away.

So why mix your own?

Esophotrast®

(barium sulfate)

Instantly ready esophageal cream

Recommended dose: 1 tablespoonful "chewed" thoroughly before swallowing. Repeat with a second tablespoonful to ensure prolonged adherence and coating of the esophageal mucosa.



Barnes-Hind Barium Products
Subsidiary of Barnes-Hind Pharmaceutica
Sunnyvale, Calif. 94086



Forget the darkroom with AUVELOPER™, the remarkable new automated x-ray processor. Auveloper accommodates a wide variety of film sizes, including PANOREX®, and all film speeds, both intra-oral and extra-oral. Auveloper eliminates hanger-loading, hand transferring of hangers from tank to tank, film drying, chemical accidents, mess and storage and all the time-consuming darkroom work. Operation is minimal. Only S. S. WHITE® has it. For details, write S. S. WHITE COMPANY, a Division of Pennsalt Chemicals Corporation, X-Ray Division, Community Drive, Great Neck, N.Y. 11021

SQUIBB

a research concept in contrast visualization

for clear definition of disease:

this oral medium is the message . . .

Oragrafin® Calcium (Squibb Calcium Ipodate) visualizes the gallbladder and ducts quickly and clearly with few undesirable reactions. For rapid or routine studies of the gallbladder and biliary ducts, Oragrafin permits efficient absorption for maximum concentration and excellent contrast—with bowel residue in only a small percentage of patients and few patient problems.

Oragrafin (Squibb Ipodate) in radiography — an advanced medium of biomedical communication. According to McLuhan's[1] provocative new theories of communications, all media are considered "extensions of man"—the means by which he extends his understanding and control of the universe and himself. In biomedical communications, where man monitors the diverse processes of molecular and cellular change, modern contrast radiography is an advanced medium.

Today, in cholangiography and cholecystography, as the medium becomes increasingly oral, the diagnostic message is clear, rapid, and convenient with Oragrafin (Squibb Ipodate).

For summary of contraindications, precautions, and side effects, see end of this advertisement.



the medium:

Oragrafin®

Squibb Ipodate

the message:

maximum concentration... excellent toleration

high absorption index—"No one will dispute the statement that the diagnostic reliability of oral cholecystography depends upon the degree of absorption of the contrast medium employed."[2] Radioisotope studies with ipodate sodium show a markedly improved absorption index (approximately 70 per cent) with no increase in the toxic properties.[2]

excellent opacification—"In addition to its ease of administration and safety, its principal advantages are a high yield of diagnostic films...."[3]

less bowel residue—"Incomplete and variable absorption of a cholecystographic agent is not desirable, for the opacification of the gallbladder is then less dependent on the status of the gallbladder and more a reflection of the percentage absorption."[4]

"Opaque material in the bowel was found in 46 per cent of [105 patients in] the...[iopanoic acid] group as compared with 9 per cent of those [99] of the [Oragrafin Sodium Capsules]...group."[4] In another study, 49 of 100 patients receiving iopanoic acid had residue in the gastrointestinal tract, while only 15 of 100 patients receiving Oragrafin Sodium Capsules had such residue.[5]

no evidence of nephrotoxicity, infrequent side effects—In contrast to findings with other cholecystographic agents, Lewitan and Garcia[6] reported in their 246-patient study: "With ipodate calcium... there was no clinical evidence of immediate or delayed nephrotoxicity in any of the patients given it...."[6] To study possible renal toxicity, "Creatinine clearance tests were also done before and after administration of multiple doses in excess of 6 gm. in 8 cases, and showed no significant alterations."[6] However, "Multiple doses beyond 6 gm. are not recommended."[6]

In their study of 120 patients, Glenn and O'Brien reported "...no reactions in this series of patients attributable to the administration of [Oragrafin]...."[3]

And, McCrory reported that Oragrafin Sodium and Calcium was "...used routinely in cholecystographic studies in approximately 2000 patients with excellent diagnostic films and only rare and mild reactions."[7]

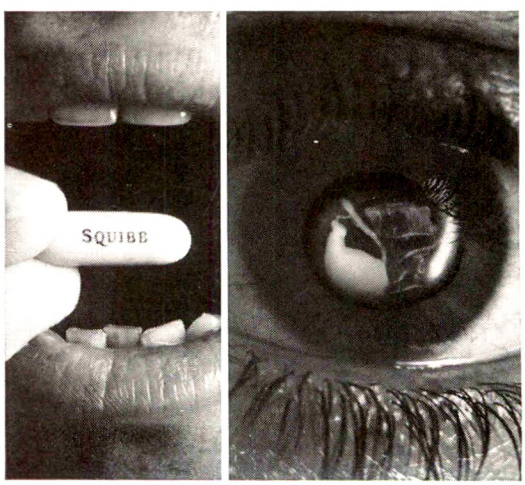
fewer side effects than iopanoic acid—According to White and Fischer,[4] 36 (36.4%) instances of side effects occurred in 99 cases with Oragrafin Sodium, 3 Gm. compared with 87 (82.9%) in 105 cases with iopanoic acid, 3 Gm. Kinds of side effects noted were nausea, vomiting, diarrhea, cramps and dysuria—all less frequent with Oragrafin Sodium (Squibb Sodium Ipodate).

Juhl,[5] in his study of 200 patients (100 on iopanoic acid and 100 on sodium ipodate), found that the incidence of nausea and vomiting was equal in the two groups.[5]

Oragrafin (Squibb Ipodate) dosage schedules
Oragrafin (calcium or sodium ipodate) permits overnight cholecystography and cholangiography.

	Gallbladder Films		Films of the Gallbladder and Biliary Ducts
11 P.M.	6 Capsules OR (or 12 Capsules)	1 packet of Granules (or 2 packets)	6 Capsules (or 1 packet of Granules, if preferred) and
next morning 8 A.M.			1 packet of Granules
9 A.M.	Visualization of gallbladder	Visualization of gallbladder	Visualization of ducts and gallbladder
10 A.M.			
11 A.M.			

For summary of contraindications, precautions, and side effects, see next page.



speed and convenience of Oragrafin® Calcium Granules

Squibb Calcium Ipodate

new clinical study[8] demonstrates improved diagnoses with calcium ipodate—"A group of 114 patients with poorly filled gallbladders after routine administration of iopanoic acid were given 6 gm. of [calcium] ipodate granules immediately following their routine cholecystography. In 66 per cent of these patients opacification of the gallbladders was obtained within 3 hours, allowing a definite diagnosis. Of the remaining 33 per cent, one-half were ultimately proven diseased." "It is apparent that many poorly visualized gallbladders can be rendered visible by the ingestion of ipodate granules.... A whole day may be saved and other diagnostic studies may be performed."[8]

patient convenience—Routine cholecystography night-before procedure is easy for patients to follow; palatable granules further enhance patient acceptability. Rapid clearance of medium permits same-day administration and gallbladder and ductal films, and if necessary, same-day re-examination; reduces need for I.V. studies.

rapid absorption permits same-day re-examination—To determine the cause of nonopacification after routine cholecystography using 6 capsules, physicians may require re-examination by repeating the procedure at a later date (sometimes doubling dose to 12 capsules), or by administering more agent the evening of the first unsuccessful examination (again sometimes doubling dose to 12 capsules), and repeating the study the next day. "The advantage of the calcium ipodate method is that the examination can be completed in five additional hours with a limited dose of contrast agent."[9]

"a valuable medium for peroral cholegraphy"[6]—Rapidly absorbed from the gastrointestinal tract, calcium ipodate has been reported by some investigators to be diagnostically superior to other oral cholangiographic contrast agents.[10,11] With careful timing of the examination and the use of tomograms or laminograms, the frequency of good results can approximate that obtained with intravenously administered agents.[10] According to Lewitan and Garcia,[6] the medium's relative safety makes it a valuable medium for peroral cholegraphy. Timesaving and economical Oragrafin Calcium Granules may be particularly useful in certain patients for whom I.V. radiography presents potential hazards, such as elderly patients and those with cardiovascular disease.

Unique among oral media, Oragrafin Calcium Granules permits same-day films of the gallbladder and the ductal system.

dosage schedule for films of gallbladder and ductal system

8 A.M.	2 packets of granules
9 A.M.	visualization of ducts
10 to 11 A.M.	visualization of gallbladder

Contraindications: Contraindicated for persons sensitive to oral iodine compounds or for patients with *combined* renal and hepatic disease or *severe* kidney impairment. Gastrointestinal disorders, which may interfere with absorption, or liver dysfunction, which may result in inadequate biliary secretion of medium, are likely to result in unsatisfactory visualization.

Precautions and Side Effects: Mild and transient nausea, vomiting, or diarrhea sometimes occur; but the incidence can be reduced by using the calcium granules and restricting the dosage to 3 Gm. Transient headache, dysuria, or abdominal pains may occur.

Hypersensitivity reactions may include urticaria, serum sickness-like reactions, and rarely anaphylactoid shock. They are more likely to occur in the individual with a history of allergy, asthma, hay fever, or urticaria and in the individual who is known to be hypersensitive to iodine compounds. Antihistamines and corticosteroids are used to control hypersensitivity reactions; but the occasional serious anaphylactoid reactions require the immediate use of epinephrine or phenylephrine, oxygen, and intravenous corticosteroids.

For full information see Package Insert.

Supply: The calcium salt (Oragrafin Calcium Granules) is available in single-dose foil packets providing 3 Gm. of calcium ipodate as Granules dispersed in flavored sucrose. The sodium salt is available in capsule form (Oragrafin Sodium Capsules) providing 0.5 Gm. sodium ipodate per capsule.

References: 1. McLuhan, M.: Understanding Media: The Extensions of Man, New York, McGraw-Hill Book Company, 1966. **2.** Sanen, F. J.: Amer. J. Roentgen. *88*:797 (Oct.) 1962. **3.** Glenn, J. C., Jr., and O'Brien, P. S.: Southern Med. J. *56*:167 (Feb.) 1963. **4.** White, W. W., and Fischer, H. W.: Amer. J. Roentgen. *87*:745 (April) 1962. **5.** Juhl, J. H., *et al.*: Radiology *80*:87 (Jan.) 1963. **6.** Lewitan, A., and Garcia, J. F.: Amer. J. Dig. Dis. *10*:219 (March) 1965. **7.** McCrory, E.: J. Tenn. Med. Ass. *58*:258 (Aug.) 1965. **8.** Root, H.: Amer. J. Roentgen. *101*: 621 (Nov.) 1967. **9.** Crummy, A. B.: Wisconsin Med. J. *65*:84 (Feb.) 1966. **10.** Saltzman, G. F.: Acta Radiol. *54*: 417, 1960. **11.** Ludin, H., and Lauchenauer, C.: Schweiz. Med. Wochenschr. *90*:471, 1960.

for clear definition of disease: in oral cholangiography and cholecystography

Oragrafin®

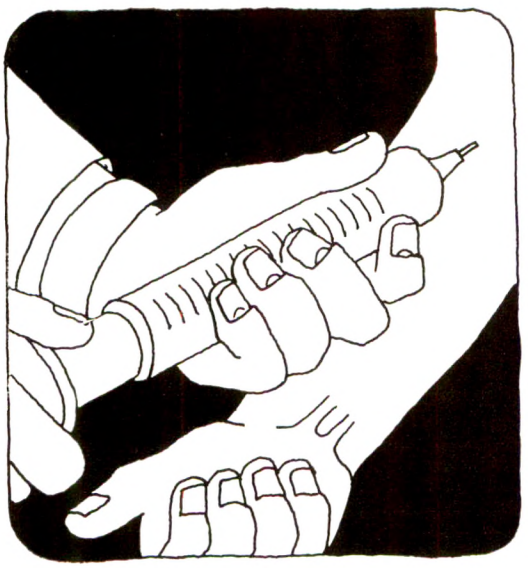
Squibb Ipodate

SQUIBB

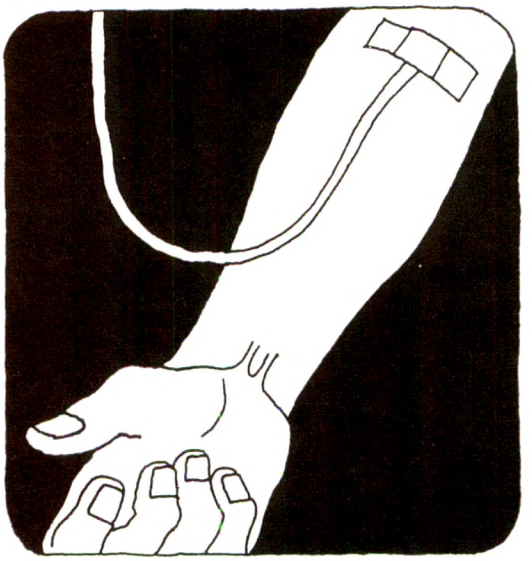
'The Priceless Ingredient' of every product is the honor and integrity of its maker.

A 2810

Now...2 important I.V. Radiodiagnostic procedures for improved visualization



Adequate Dose Urography
with 50-60 ml. of 50% solution



Drip Infusion Pyelography
using between 250-400 ml. of a 25% solution*

Hypaque® 50%

sodium

brand of **sodium diatrizoate**

Winthrop

PIONEERS IN PRODUCTS FOR RADIOLOGIC DIAGNOSIS

*By diluting the 50% solution with an equal amount of sterile water for injection, USP, sodium chloride injection, USP, or dextrose injection, 5%, USP.

(Please see summary on following pages)

Hypaque® 50%
sodium
brand of **sodium diatrizoate**

Excretory Urography and Drip Infusion Pyelography

Description: Hypaque sodium is a sterile aqueous solution of sodium 3,5-diacetamido-2,4,6-triiodobenzoate, a radiopaque medium used to delineate internal structures.

Warning: Do not use Hypaque sodium for myelography. Injection of even a small amount into the subarachnoid space may produce convulsions and result in fatality.

General and Specific Precautions: Caution is advised in patients with a history of bronchial asthma, other allergic manifestations, or of sensitivity to iodine; these conditions represent a special risk, though not an absolute contraindication. To avoid or minimize possible allergic reactions, premedication with antihistamines may be considered. Benadryl (diphenhydramine hydrochloride) in the same syringe with Hypaque may result in precipitation. A test dose of contrast medium is not entirely reliable. Severe reactions, including fatalities, have occurred with a test dose as well as with the full diagnostic dose.

Caution is advised in patients with severe cardiovascular disease. In patients with impaired renal function and cardiovascular disease, drip infusion pyelography imposes a sudden osmotic and sodium load which can precipitate congestive heart failure. Contrast media injected into arteries or veins can promote sickling of red cells in susceptible individuals. In patients with reduced renal function, repeat of excretory or retrograde pyelography should be delayed at least 48 hours to avoid temporary suppression of urine. In preparation for excretory urography of patients with multiple myeloma, partial dehydration is not recommended, since this may predispose to the precipitation of myeloma protein in the kidney tubules. When thyroid function studies (PBI and 24-hour radioiodine uptake levels) are indicated, they should be performed *prior* to radiographic studies or several days afterwards, to avoid inaccurate results.

Hypaque sodium 50% should always be injected at body temperature.

General and Specific Adverse Reactions: Adverse reactions, usually of a minor nature, have occurred in 10-14 per cent of patients who have received Hypaque intravenously. Reactions due to *faulty technique* include hematomas and ecchymoses, following extravasation from the vein, and pyrogenic reactions. *Hemodynamic reactions* include vasodilatation with flushing, hypotension and, rarely, vein cramp or thrombophlebitis. Serious *cardiovascular reactions* include rare cases of cardiac arrhythmias (e.g., ventricular fibrillation), shock, and cardiac arrest. Transient proteinuria may occur occasionally following the injection of radiopaques and, rarely, oliguria and anuria have been reported secondary to a hypotensive reaction. *Allergic reactions* include asthmatic attacks, nasal and conjunctival symptoms, cutaneous reactions such as urticaria and, rarely, anaphylactic shock, sometimes with fatal outcome. Severe reactions may also be manifested by signs and symptoms relating to the *respiratory system* (dyspnea, cyanosis, pulmonary or laryngeal edema), or to the *nervous system* (restlessness, confusion, or convulsions). *Other reactions* include nausea, vomiting, excessive salivation, anxiety, headache, and dizziness. Infrequently, "iodism" (salivary gland swelling) from organic compounds appears two days after exposure and subsides by the sixth day. Reactions to drip infusion pyelography may not appear until some hours after the examination.

Angiography (Peripheral Arteriography and Venography)

Precautions *(See also General Precautions):* Extreme caution is advised in considering peripheral arteriography in patients suspected of having thromboangiitis obliterans (Buerger's disease). Any procedure (even needling or insertion of a catheter) may induce a severe arterial and/or venous spasm. Caution is also advisable in patients with severe ischemia associated with ascending infection.

Adverse Reactions *(See also General Adverse Reactions):* In addition to those listed under General Adverse Reactions, are those due to arterial trauma during the procedure (i.e., needling, insertion of catheter, subintimal injection, perforation, etc.) as well as to the hypertonicity or effect of the medium; also reported are transient arterial spasm, extravasation, hemorrhage, hematoma with tamponade, injury to nerves proximal to artery, thrombosis (rare in venography; if vein is irrigated following injection), dissecting aneurysm, arteriovenous fistula, (e.g., with accidental perforation of femoral artery and vein during needling) transient leg pain from contraction of calf muscles in femoral arteriography; transient hypotension after intraarterial (brachial) injection, and brachial plexus injury with axillary artery injections.

Cerebral Angiography: Because of the special techniques required, it is recommended that Hypaque sodium be used for this purpose only by persons skilled and experienced in carrying out this procedure.

Contraindication: Carotid angiography should be avoided during the progressive period of a stroke, since this increases the risk of cerebral complications.

Precautions *(See also General Precautions):* Select patients for this procedure with care. Use the 50 per cent solution with caution in extreme senility (but not old age, *per se*); advanced arteriosclerosis; severe hypertension; and cardiac decompensation.

The diagnostic value of the procedure, according to many authorities, when employed early enough in locating lesions amenable to surgery, may outweigh the added risk to patients who have recently experienced cerebral embolism or thrombosis (stroke syndrome). A small number of postangiographic fatalities, including progressive thrombosis, have occurred in which the procedure did not appear to play a role. Patients with severe cerebrovascular disease may be examined primarily by indirect methods of angiography.

Care should be exercised to avoid contaminating catheters, syringes, needles, and contrast media with glove powder or cotton fibers.

Angiography is hazardous in subarachnoid hemorrhage. In migraine, the procedure can be hazardous because of ischemic complications, particularly if performed during or soon after an attack.

Adverse Reactions *(See also General Adverse Reactions):* The major sources of complications are faulty technique, occlusive atherosclerotic vascular disease, repeated injections of the contrast media, and higher doses than those recommended.

Untoward reactions are mostly mild and transient, although permanent visual field defects and deaths have been reported.

(continued on next page)

(continued from preceding page)

Hypaque® 50%
sodium
brand of **sodium diatrizoate**

Vascular reactions: flushing, vessel spasm, thrombophlebitis, and cutaneous petechiae.

Neurologic complications: transient cerebral blindness, neuromuscular disorders, convulsions, coma, hemiparesis, unilateral dysesthesias, visual field defects, aphasia, and respiratory difficulties.

Aortography

Precautions *(See also General Precautions):* Special caution is advised to avoid inadvertent intrathecal injection when using the translumbar technique. The incidence and severity of reactions or complications that may occur are influenced by: the care and experience with which the procedure is performed; the amount and type of medium used; the age and condition of the patient; and the premedication and anesthesia used. Since aortography is not without some danger, it should be performed only by those experienced in the technique. Wherever possible, repeated injections of the solution during a single study should be avoided.

Adverse Reactions *(See also General Adverse Reactions):* Renal damage and shutdown; neurologic complications such as transverse myelitis or paraplegia; cardiovascular complications such as shock, cardiac arrest or failure, coronary occlusion, arterial thrombosis, embolism, and perforation of vessels; extravasation or hemorrhage from the puncture site or retroperitoneal catheter perforation; necrosis of the intestinal wall; acute pancreatitis; deaths; diffuse cutaneous petechiae; subintimal injection and aortic dissection.

Intraosseous Venography

See General Precautions and Adverse Reactions. A general anesthetic is sometimes necessary since the method is painful. Occasionally, extravasation of the contrast medium from the needle into the soft tissue may occur.

Direct Cholangiography

Precaution *(See also General Precautions):* This procedure should be used with caution in the presence of acute pancreatitis, injecting no more than 5 to 10 ml. without undue pressure.

Adverse Reactions *(See also General Adverse Reactions):* These may be attributed to injection pressure or excessive volume of the medium, resulting in overdistention. Such pressure may produce a sensation of epigastric fullness, followed by moderate pain in the back or right upper abdominal quadrant, which will subside when injection is stopped.

Some of the medium may enter the pancreatic duct and cause a transient serum amylase elevation 6 to 18 hours later, without apparent ill effects. Pancholangitis resulting in liver abscess has been reported. Occasionally, nausea, vomiting, fever, and tachycardia have been observed.

Hysterosalpingography

Contraindications: Menstruation, active or imminent; infection in any part of the genital tract, including the external genitalia; pregnancy, known or suspected. Use not advised for six months after end of pregnancy, or 30 days after conization or curettement.

Precaution *(See also General Precautions):* Caution should be exercised in patients with known or suspected carcinoma to avoid possible spread of the lesion by the procedure.

Splenoportography

Precautions *(See also General Precautions):* Procedure should be performed with caution on patients with blood dyscrasias, a tendency to severe bleeding, or a spleen recently become tender and palpable.

Adverse Reactions *(See also General Adverse Reactions):* Persistent hemorrhage with hemoperitoneum has been reported, and, in some instances, hemorrhage has required splenectomy.

How Supplied: Ampuls of 30 ml., boxes of 1, 10, and 25. A 1 ml. sensitivity test ampul is furnished with each ampul. Vials of 20 and 30 ml., rubber stoppered, boxes of 1, 10, and 25. Vials of 50 ml., rubber stoppered, boxes of 1 and 10. Each vial contains sufficient excess to permit withdrawal of 1 ml. for testing sensitivity.

If the solution is chilled, crystals may form but will readily dissolve if the ampul or vial is placed in moderately hot water before use. Cool to body temperature before injecting.

Winthrop

WINTHROP LABORATORIES, New York, New York 10016

PIONEERS IN PRODUCTS FOR RADIOLOGIC DIAGNOSIS



W. G. COSBIE, M.B.
Janeway Lecturer, 1968

CALCU
CENTRAL
LIBRARY
UNIVER

THE AMERICAN JOURNAL OF ROENTGENOLOGY
RADIUM THERAPY AND NUCLEAR MEDICINE

VOL. 105 MARCH, 1969 No. 3

THE CENTRALIZATION OF CANCER SERVICES—HOW FAR SHOULD IT GO?*

THE JANEWAY LECTURE, 1968

By W. G. COSBIE, M.B.
TORONTO, ONTARIO, CANADA

As I have come to know something of Dr. Henry Janeway, the man and his work, I have realized how great an honor it is to deliver this Memorial Lecture before this Society.

Dr. Janeway was truly a pioneer in radiotherapy when he began his great work in 1910, and his numerous achievements in the short period of 11 years, plagued by ill health that would have broken a less courageous spirit, demonstrate clearly that time alone is not a major factor in the career of a dedicated genius. He was a well-trained and competent surgeon, and experience soon taught him the necessity to explore every avenue of therapeutics to lessen the number of incurables. He had a practical knowledge of the anatomic problems of extending malignancies, and when he was faced with the technical difficulties of radium applications he mastered them with a craftsmanship unique at any time.

Dr. Janeway spent his productive years on the staff of the Memorial Hospital and undoubtedly the associations he developed presented to his fruitful mind a constantly stimulating challenge. One can imagine the great interest he would have taken in the subject of this Lecture, and the contributions he would have made had he lived 50 years later than he did.

INTEREST in the question of centralization of cancer services has greatly increased as a result of the work of the Sub-Committee on Cancer of the President's Commission on Heart Disease, Cancer and Stroke, which was presented in a report in February 1965. The recommendations of the Sub-Committee are well known to most of the members of this Society and many have given considerable thought as to the means by which they might be implemented.

There was a time within the memory of some of us when the control of disease and the care of the sick was the prerogative and sole responsibility of the medical profession. The doctor with his little black bag and the community hospital were usually capable of providing all the services which

* Presented at the Fiftieth Annual Meeting of the American Radium Society, Miami Beach, Florida, April 7–11, 1968.

were considered necessary. Not long after the advent of radium, however, it became increasingly evident that the expense entailed to develop the full potentials of the new therapy required the support of private philanthropy or government finance, and on this basis special centers developed in this country, Great Britain and Western Europe.

It is interesting to compare the program which has developed in Ontario during the last 35 years with the recommendations of the Sub-Committee on Cancer. In Canada, health administration is a provincial jurisdiction. The Federal Government, in making various health grants to the provinces, confines its influence to guidelines as to how the money shall be spent.

Ontario has a population of over 7,250,000 people living in an area of 412,582 square miles. Toronto, the largest city, has a population of nearly 2,000,000, and Ottawa and Hamilton both have populations of about 500,000. Western Ontario is a rich farming country with many small cities and good-sized towns. Northern Ontario, of vast extent, is sparsely populated—a land of gold, iron, nickel and uranium mines—of pine forest and innumerable lakes.

In 1931 a Royal Commission was appointed by the Ontario Government "to enquire into the use of radium and X-rays in the treatment of the sick." While there had been some radiotherapy ever since Dr. W. H. B. Aikins, the first President of this Society, brought the first radium to Canada in 1910, apart from the work of Dr. Gordon Richards at the Toronto General Hospital, it was primitive, uncertain and of very limited value. So it was a very opportune time to consider the need for government support if the people of Ontario were to benefit from this important type of therapy.

The Commission, under the Chairmanship of the Minister of Education, the Rev. H. J. Cody, who later became the President and then the Chancellor of the University of Toronto, consisted of Sir John McLennan, one of Canada's leading scientists and Professor of Physics at the University of Toronto, Dr. W. T. Connell, Professor of Medicine of Queen's University, Kingston, and Arthur Ford of London, Ontario, a newspaper editor and later the Chancellor of The University of Western Ontario. They were accompanied on a tour of inspection by the Minister of Health and his Deputy. After holding meetings in Ontario with representative groups of physicians, surgeons, radiologists and pathologists, the Commission visited leading cancer and radiotherapy centers in this country, Great Britain, Germany and Belgium, Paris, Copenhagen and Stockholm. Almost everywhere they received the same advice—to concentrate on a few first-class centers, preferably associated with the universities, where highly trained radiotherapists might have the support of good radiation physicists. Research facilities were essential, and full co-operation between surgeons and radiotherapists was absolutely necessary if the best results were to be obtained. Diagnostic clinics should be encouraged in hospitals which would refer the patients to the treatment centers, and the education of the profession and the public was the basis for early diagnosis and a hope of curing more patients. In a comprehensive report of 170 pages, the Commission recommended that the Government should provide financial support for the purchase of radium and x-ray equipment, and should establish a cancer institute, either as a separate institution or associated with a general hospital, not only for diagnosis and treatment but also for research. It recommended establishment of a number of active treatment centers which, in the beginning, should be associated with the teaching hospitals of the three medical schools. It advised that doctors, nurses, dentists, teachers, the press and the public should be asked to co-operate in an educational campaign, and that the program of cancer control should be entrusted to a commission which would inaugurate and supervise the active treatment and diagnostic clinics in order to secure close co-

operation of all services in the treatment of cancer.

After a long gestation period, The Ontario Cancer Treatment and Research Foundation was incorporated in 1943 to conduct a program of diagnosis, treatment and research in cancer including: (a) the establishment of a hospital center with facilities for diagnosis and treatment; (b) the laboratory and clinical investigation of cancer problems; (c) the co-ordination of facilities for treatment; (d) the establishment of diagnostic centers in general hospitals or elsewhere; (e) the adequate reporting of cases and the recording and compilation of data; (f) the education of the public in the importance of early recognition and treatment; (g) the providing of facilities for undergraduate and postgraduate study; (h) the training of technical personnel; (i) the providing and awarding of research fellowships; and (j) the transportation of patients and necessary escorts to treatment centers for diagnosis, treatment and investigation.

The Foundation is a lay board, appointed by the Government on a Province-wide basis, responsible, through its Chairman, to the Minister of Health. It is advised by a medical board under the chairmanship of the Medical Director of the Foundation.

In the otherwise latent period, grants were made not only to the clinics in Toronto, Kingston and London, but also to radiotherapy or tumor clinics in Hamilton, Ottawa and Windsor which had developed on a basis of local interest. Of equal importance was the institution in 1937 of a record system by Dr. A. H. Sellers, the Statistician to the Ontario Department of Health, who received very valuable help and advice from Dr. Richards and Dr. Norman McCormick of Windsor, who will be remembered as a Past President of this Society. This system applied to the 6 centers and has been maintained ever since.

In the 8 years between 1946 and 1954, the Foundation assumed the responsibility for the maintenance of the regional radiotherapy centers, to which another had been added, in Port Arthur, at the Lakehead, because of its geographical location. Substantial building grants were made to the hospitals where the clinics were located in order to provide suitable accommodation, cobalt 60 and x-ray therapy units were installed, and an adequate supply of radium was provided. At the same time the Foundation came to an agreement with the hospitals that they would set aside a sufficient number of beds to accommodate the patients who would be under treatment in the clinics. The Foundation also became responsible for the financial support of the staffs of the clinics—professional, technical, nursing and clerical. Through an agreement with the medical schools and the hospital boards, the clinic directors have been recognized as heads of the departments of radiotherapy and/or radiotherapists-in-chief to the hospitals concerned, and their associate radiotherapists, of whom there are now 27, also hold university and/or hospital appointments. Consultants in the various medical and surgical specialties have also been appointed to the clinics on the recommendation of the heads of the clinical departments or the hospital medical boards.

From the beginning it was planned that the Clinic at the Toronto General Hospital would become the Cancer Institute of Ontario. Even as early as 1931, Dr. Richards had developed an efficient radiotherapy service and good co-operative clinics with his consultants who were senior members of clinical departments, and the patients profited, not only by their advice but also by their surgical skill when operative treatment was undertaken. Inadequate accommodation, however, had become an increasingly serious problem and it was obvious that this must be rectified. A committee, under the Chairmanship of the President of the University, considered the question of a new building where radiotherapy for all the teaching hospitals could be developed, and after prolonged study the University joined with the Foundation in preparing plans which were eventually ac-



FIG. 1. The Ontario Cancer Institute and Princess Margaret Hospital, Toronto, Ontario, 1968.

cepted by the Provincial Government. The result was that The Ontario Cancer Institute, embodying the Princess Margaret Hospital, was built and opened in 1958 (Fig. 1). It was incorporated by the Government and operates under a Board representing the Foundation and the University, and with representatives from the general hospitals associated with the Medical School, the Board being responsible through its Chairman to the Provincial Minister of Health. It was recognized as a teaching hospital of the University, and Dr. Clifford Ash, who had succeeded Dr. Gordon Richards at the Toronto General Hospital, became the Director of the Institute.

Even before the building was opened, Dr. Ash was assisted by Professor Harold Johns and Professor Arthur Ham in assembling a permanent research staff for the Institute, consisting of radiation or biophysicists and a group of biologists with a very broad range of interests. Thus there evolved something new in Toronto, and the University, realizing the great potentials not only for cancer research but for the training of graduate and undergraduate students, established the Department of Medical Biophysics with its headquarters in the Institute.

Although the Institute was primarily for radiotherapy, accommodation was provided for intense clinical investigation and a Department of Medicine, including Pediatrics, was organized. The close association between clinical and fundamental investigators which developed has given the Institute an outstanding place in Canadian medicine and offers even better promise for the future. To accommodate expanding activities, major additions have been added to the Institute and Hospital so that there are now 175 beds, of which 25

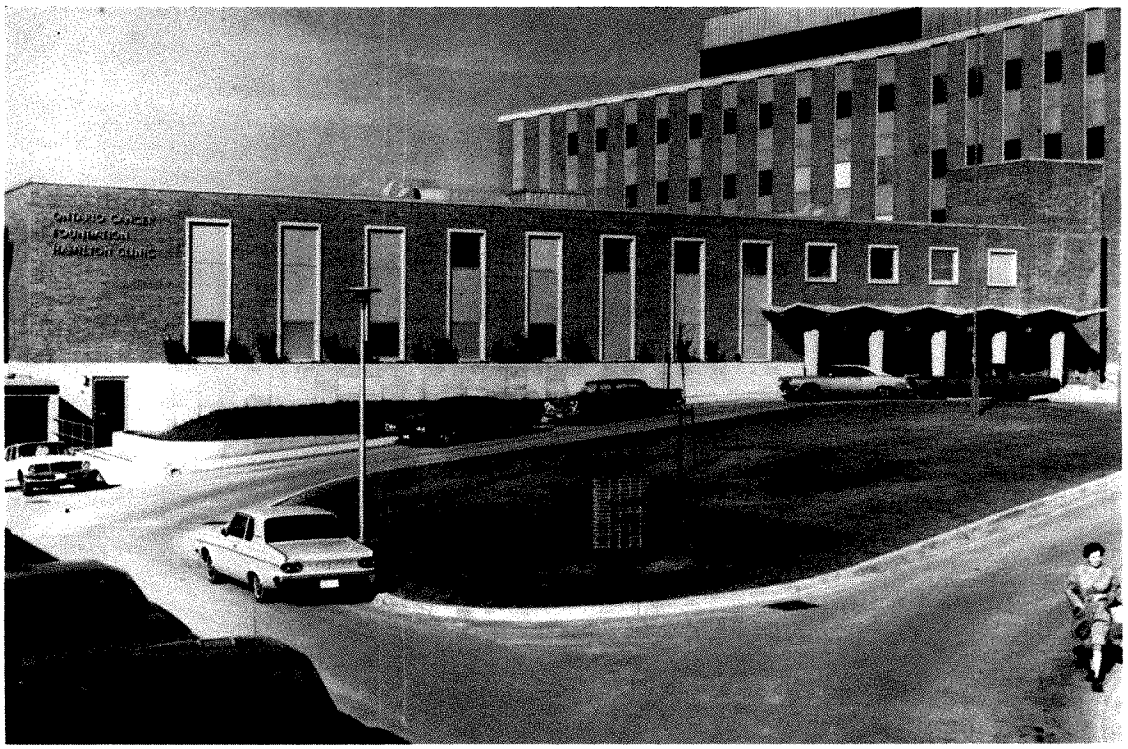


Fig. 2. The Ontario Cancer Foundation Hamilton Clinic, Hamilton, Ontario.

comprise a Pediatric Unit and 30 are assigned to the Department of Medicine. With further research facilities to provide for a growing number of biologists and biophysicists, the opportunity for combined investigation is unique in Canada.

Also an important feature of the work at this Institute has been the development of considerable original equipment, both for therapy and diagnostic purposes.

The therapy equipment at the Institute includes a 24 mev. betatron unit, 6 cobalt 60 teletherapy units, 2 cesium therapy units and standard x-ray equipment. All the regional clinics have a full range of therapy equipment, including cobalt 60 units, and, in addition, the London Clinic has a 35 mev. betatron unit and facilities for hyperbaric oxygen therapy, the Hamilton Clinic has a 6 mev. linear accelerator, and in Ottawa, through arrangements with Atomic Energy of Canada, a special room has been provided where the latest therapy equipment produced by this company is installed and given its first clinical trials. In addition, as a result of the growing importance of hormone and chemotherapy, specially trained physicians have been appointed on a full or half-time basis to the staffs of the regional clinics, with the approval of the medical schools or the hospitals concerned (Fig. 2 and 3).

It is reasonable to claim that radiotherapy is centralized in Ontario. This seems a natural development, as with the coming of the well-trained physician radiotherapist* spending all his time treating large numbers of patients, modern radiotherapy has passed beyond the scope of the diagnostic radiologist whose major interests have also become highly specialized. It has become a free service under the Ontario Hospital Services Commission which reim-

* The Royal College of Physicians and Surgeons of Canada awards Fellowships in the Royal College of Physicians (F.R.C.P. (C)), after a very broad examination, to therapeutic radiologists who have had 5 years of satisfactory postgraduate training. Similarly, at a lower academic level, certificates are granted recognizing separate specialties in therapeutic and diagnostic radiology.



FIG. 3. New Wing of Victoria Hospital, London, Ontario, with three floors to accommodate the Ontario Cancer Foundation London Clinic.

burses the Foundation and the Institute for services rendered both to in and out-patients, and the Foundation provides free transportation to the centers. The volunteers of the Canadian Cancer Society, driving their own cars, provide a daily service to the centers for out-patients.

The volume of work in the various centers is indicated in Table I.

Major factors in maintaining the program of centralization are the consultative and follow-up clinics which have been organized in relation to the various centers. There are now 22 of these clinics located in general hospitals in 19 cities and towns. In 3 places, 2 clinics have been developed to satisfy community and church hospitals, and it is interesting that the clinic in the small town of Wingham, because of its central location, provides services for a number of much larger communities. They are visited at regular intervals by radiotherapists from the main centers, and the local physicians and surgeons feel that they have a continuing interest in their patients. They also provide an opportunity for primary consultations and, as a result, in

TABLE I

ONTARIO CANCER FOUNDATION, 1966

Regional Clinics	New Cancer Cases Registered*
Princess Margaret Hospital	3,617
Hamilton	1,454
Kingston	590
London	1,586
Ottawa	919
Thunder Bay	162
Windsor	507
Total	8,835

* In addition, 25,441 cases registered in previous years were seen at the Clinics in 1966.

1966, 736 patients were referred from these clinics to the treatment centers. A few years ago a number of diagnostic clinics were organized in Northern Ontario, but only 2 remain, as the consultative clinics, although they demand the valuable time of a radiotherapist, are proving much more acceptable. Table II has been prepared to show the size of the medical communities immediately affected by the local consultative clinics, and Figure 4 indicates the areas in the Province from which patients go to the various treatment centers.

Since 1948 financial support has been given to a Cancer Detection Clinic which was organized by the staff of the Women's College Hospital, Toronto. Over 30,000 women have attended this Clinic. A nominal charge is made for the examination and the Foundation underwrites the annual deficit. Experience has shown, however, that a clinic of this type is in danger of becoming limited in its effect by the large number of return visits of patients, and its chief value would appear to be a demonstration of the fact that some early cancers can be diagnosed in the absence of symptoms.

To encourage early diagnosis, since 1951 the Foundation has subsidized a diagnostic biopsy service for non-hospitalized patients under the care of private physicians. A special form is used, indicating that cancer is suspected, and nearly all the certified pathologists in the Province co-operate in providing the service, and from 3,500 to 4,000 practitioners make use of it. The examination of over 30,000 biopsies annually results in the diagnosis of over 3,500 malignant lesions each year.

It has been the policy in Ontario to encourage the development of cytology facilities on a Province-wide basis in order that all the major types of cytology may be available in any active treatment hospital in which there are supervised laboratories. There are at present 80 laboratories in Ontario (26 in Metropolitan Toronto) providing this service, and facilities are available in every major regional area. The Foundation has supported the training of a large number of cytotechnicians, and offers short-term scholarships to certified pathologists to cover the expense of special training in this field. Cytology has become an insured service for all patients admitted to hospital to encourage the taking of cervical smears on all female patients, and reports indicate that approximately 450,000 women had Papanicolaou smears reported on last year, 230,000 of them in Toronto. This indicates a reasonably satisfactory coverage for the female population at risk, but the major problem remains—how to reach the significantly large group of women who are never affected by this service.

Since 1964 the Foundation has supported a survey of the value of oral cytology conducted by the dentists of Ontario, under the guidance of the Faculty of Dentistry of the University of Toronto. As a result it is believed that an increasing number of dentists are becoming aware of their responsibility in the early detection of oral cancer.

Support has also been given to studies to determine the value of sputum cytology in pre-clinical cancer of the lung when it is applied in a high risk population.

Also, recently, as a result of studies of

TABLE II

ONTARIO CANCER FOUNDATION, 1967
CONSULTATIVE AND FOLLOW-UP CLINIC

Center	Doctors in Center	Center	Doctors in Center
Chatham	49	St. Catharines	152
Cornwall (2)	52	Sarnia (2)	103
Galt	37	Sault Ste. Marie	73
Guelph	73	Stratford	37
Kitchener	150	Sudbury	128
London	427	Timmins	27
North Bay	56	Welland	42
Owen Sound	35	Wingham	4
Pembroke (2)	18	Woodstock	49
Peterborough	94	Total	1,606*

* The 1,606 doctors are those in the cities and towns only. The clinics actually serve both urban and rural areas.

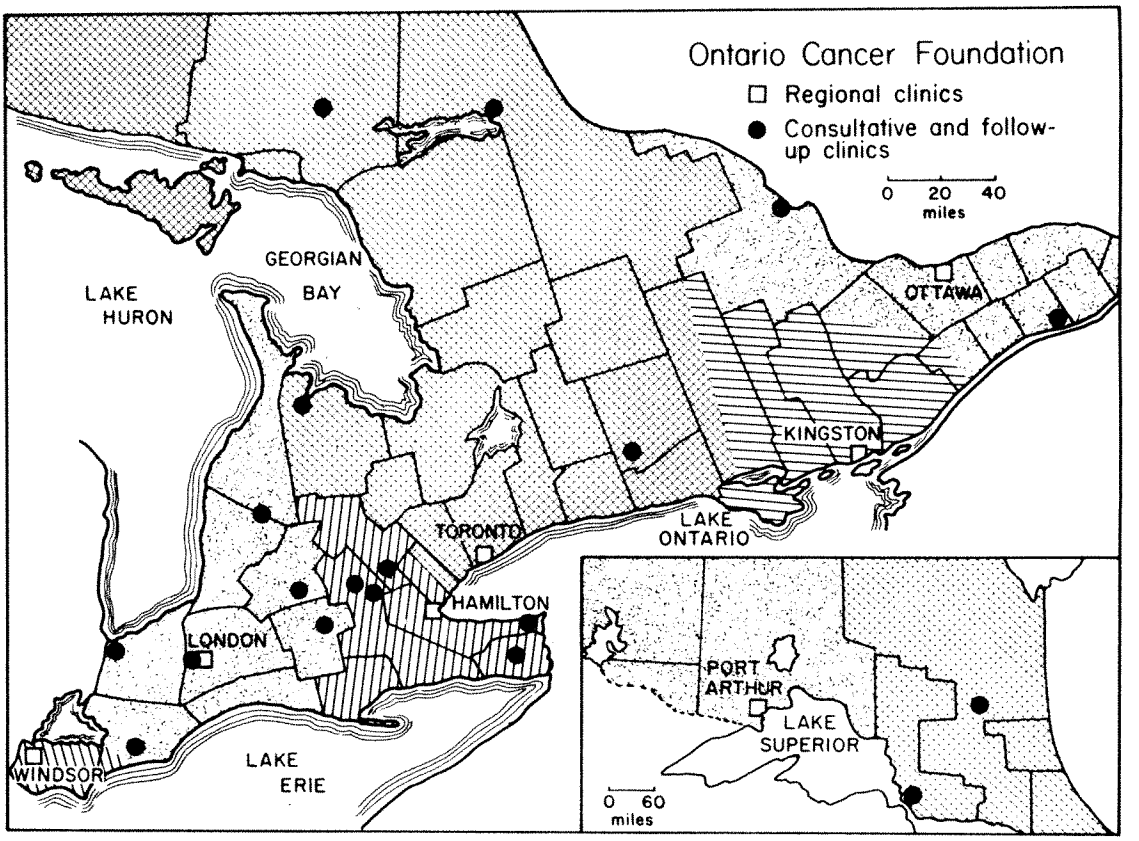


FIG. 4. Map indicating areas in the Province from which patients go to the various treatment centers.

mammography as an aid to the diagnosis of certain features of carcinoma of the breast, the Foundation is supporting short courses of instruction for radiologists in the special techniques required to give more accurate use of this diagnostic procedure.

The Foundation provides free accommodation in lodges in connection with the Princess Margaret Hospital and the clinics in London and Hamilton. The buildings and their furnishings have been provided by the Ontario Division of the Canadian Cancer Society, and similar accommodations in Ottawa, Kingston and Port Arthur only await the erection of new hospital buildings in these centers. Here, in a home-like atmosphere, ambulatory patients are accommodated under very modified supervision with daytime freedom so far as their condition will permit. The volunteers of the Cancer Society provide many features to add to the patients' comfort; hairdressing salons, moving pictures, concerts and many other diversions. An important feature in these days of constantly rising hospital costs is the minimum expense entailed in providing this accommodation (Fig. 5, 6 and 7).

In 1957 the Foundation and the Ontario Division of the Canadian Cancer Society organized a survey to determine the unmet needs of cancer patients after discharge from hospital. The survey was carried out by a senior member of the staff of the School of Nursing, University of Toronto, who was very experienced in Social Service and Public Health Nursing. It was made in Waterloo County which has a balanced urban and rural population with a low degree of indigence. As a result of a year's

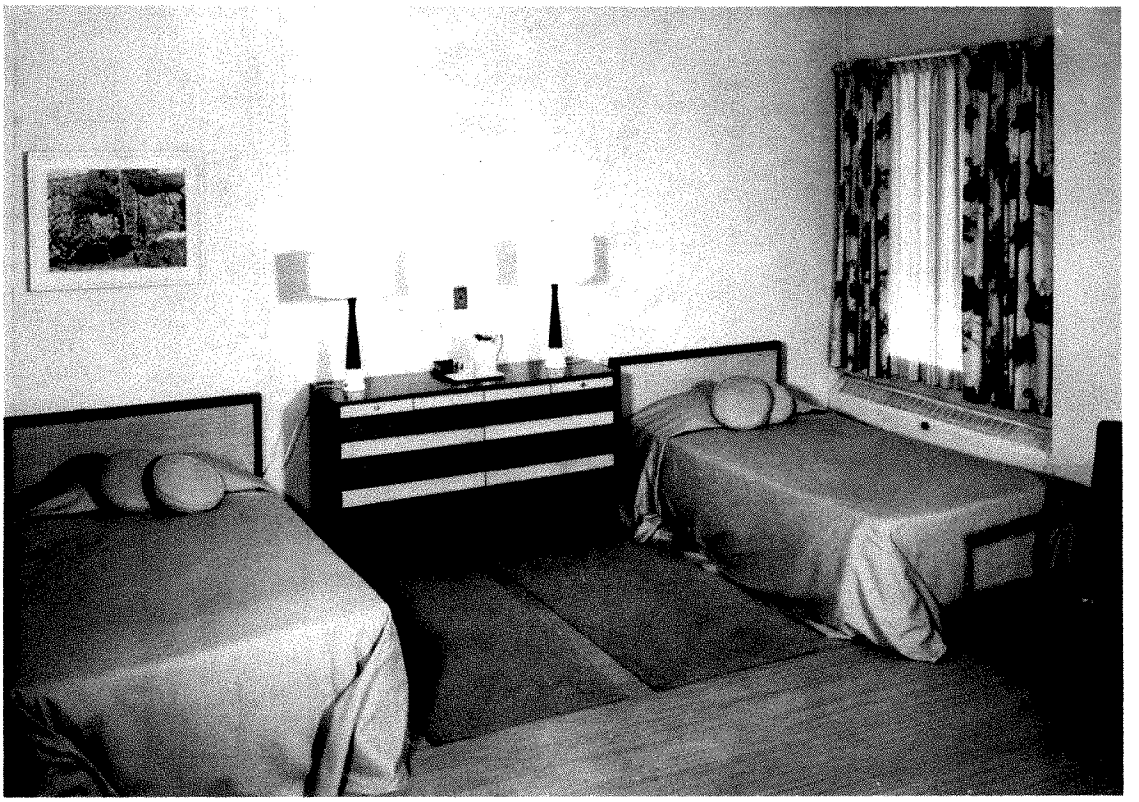


Fig. 5. Patients' Bedroom at the Princess Margaret Hospital Lodge, Toronto, Ontario.

study the Foundation established a subsidized drug service to provide special therapeutic agents to patients suffering from malignant diseases, who are at home under the care of their family doctors and who, in their opinion, are unable to pay for the drugs they require. A special prescription form is used demanding the use of generic names, previous attendance at a Foundation treatment center or the endorsement of the diagnosis and prescribed drug by a recognized consultant. Prescriptions are only filled at the Princess Margaret Hospital or at the hospital associated with a regional clinic after being endorsed by the clinic director. A committee reviews the service regularly and authorizes the list of preparations available to the prescribing physicians. In 1966, 1,274 patients under the care of 700 physicians benefited from this service. Also, as a result of the survey, the Ontario Division of the Cancer Society undertook to pay for pain-relieving drugs prescribed at local drug stores and also to maintain the services of visiting nurses and housekeepers when necessary.

In 1958 the Foundation met with representatives of the Division of Rehabilitation Medicine, University of Toronto, and the Ontario Division of the Canadian Cancer Society, and laid the plans for a speech therapy center for patients who had undergone laryngectomy. Prior to this the only instruction available had been unofficially sponsored by the Cancer Society. Now the program of expert instruction is carried on in the Lodge at the Princess Margaret Hospital, under the Division of Rehabilitation Medicine, with financial support from the Foundation. The speech therapist and her associates are specially trained in voice culture and not only have excellent results been obtained for a large number of patients, many of whom are referred from



FIG. 6. Patients' Lounge at the Princess Margaret Hospital Lodge, Toronto, Ontario.

outside Ontario, but the center has become a teaching unit in speech pathology and audiology providing a supply of speech therapists to other parts of the country. Instruction is free and the Cancer Society provides electrolarynxes to a number of patients who fail to acquire satisfactory voice. Seven years ago, co-operating with the Division of Rehabilitation Medicine, a prosthetic unit was organized. It has been of particular benefit to patients who have undergone operations resulting in marked facial disfiguration or who require intra-oral prostheses. The results have been such that over 90 per cent of the patients have been able to return to their normal occupations, and opportunity has also been taken to develop improvement in facial prostheses and intra-oral voice amplifiers. The prostheses are supplied without charge to the patients. In the Physiotherapy Department of the Princess Margaret Hospital patients suffering from post-mastectomy lymphedema are being treated and they also benefit from special prostheses provided from the prosthetic unit. The problem of occupational rehabilitation is entrusted to the Hospital Social Service Department which maintains many useful contacts.

As has already been indicated, an extensive program of fundamental cancer research is carried on at The Ontario Cancer Institute. It is supported by many fund granting bodies but the Foundation is responsible for the budget which maintains the permanent staffs. In addition, since 1944 the Foundation has supported the program of clinical research which is carried on in the Province. In the first place, this involves the appointment and support of a number of clinical research associates and fellows working in the clinical departments of the medical schools. Also, support is given for many investigations carried out by members of the De-

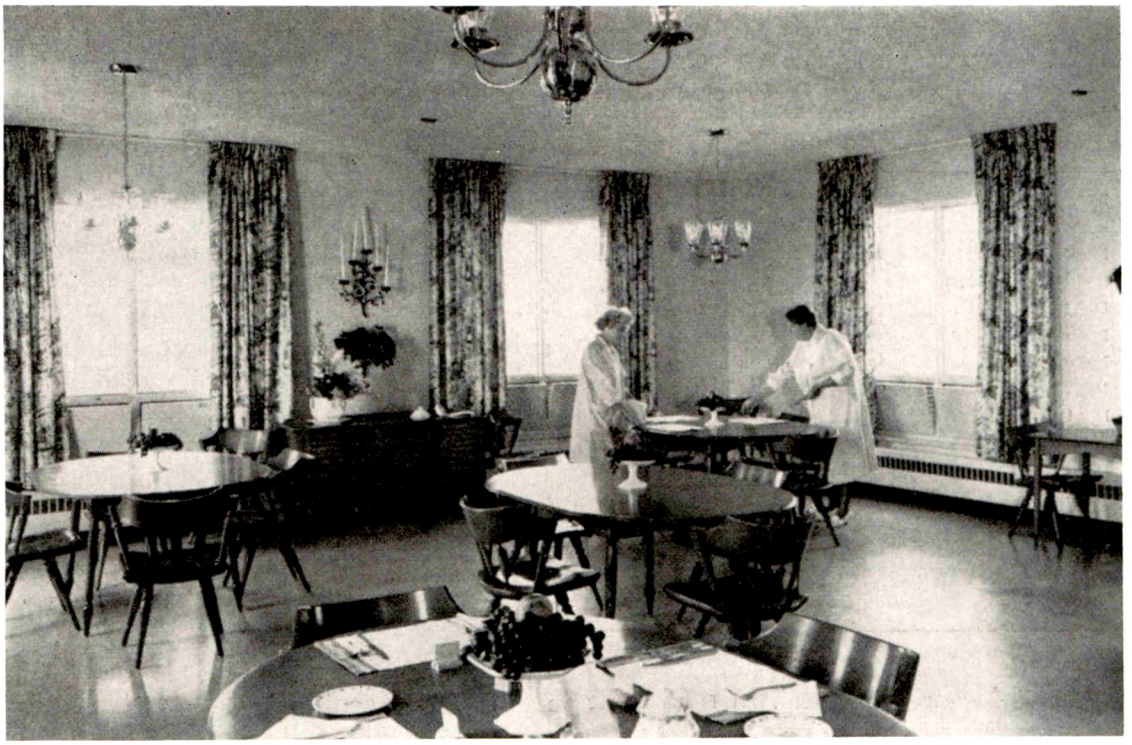


Fig. 7. Patients' Dining room at Thameswood Lodge, Ontario Cancer Foundation London Clinic, London, Ontario.

partments of Medicine, Surgery, Pathology, Gynecology and other specialties in the Provincial medical schools. These investigations are concerned with diagnostic and therapeutic problems, and also the biologic changes which are associated with malignant disease and which may influence planned treatment or indicate prognostic factors. More and more collaborative clinical trials are being organized by the clinics and hospitals within the sphere and influence of the Foundation.

The importance of the services of the radiation physicist to an efficient radiotherapy clinic cannot be overemphasized. Without his collaboration and a well-equipped machine shop, it is impossible to provide the routine services which are required. But it is also true that if the services of highly qualified radiation physicists are necessary to maintain progressive improvement in radiotherapy, then research facilities must be provided for them. On this basis, good research studies in biologic reactions and improved techniques are being supported in a number of our regional clinics.

Last year a 2 day conference was held by over 100 grantees and their assistants, where they presented the results of their investigations. There were no guest speakers on this program and it has been planned to repeat it every second year.

Dr. A. H. Sellers and his associate, Dr. Elizabeth MacKay have maintained a central bureau of statistics for the regional treatment centers and the Princess Margaret Hospital since 1937, and by the end of 1966 the records of 138,000 patients were on file. In the early years these records represented only the results of radiotherapy, but commencing in 1946 tumor registries have been supported in the general hospitals where the clinics are located, and since 1950 registries have been organized in 7 hospitals in Toronto associated with the

TABLE III

ONTARIO CANCER FOUNDATION
CLINICAL CONFERENCES

Year	Location	Site	Volume
1954	Windsor	Corpus uteri	960
1954	London	Bladder	606
1955	Hamilton	Intrinsic larynx	224
1956	Kingston	Tongue	677
1957	Toronto	Hodgkin's disease	960
1958	Windsor	Intra-oral	1,548
1959	London	Cervix uteri	4,994
1960	Hamilton	Paranasal sinus	307
1961	Kingston	Lung	2,457
1962	Ottawa	Lip	4,069
1963	Toronto	Breast	11,393
1964	Port Arthur	Testicle	827
1965	Windsor	Ovary	1,983
1966	London	Leukemia	1,520
1967	Hamilton	Central nervous system	1,142

Princess Margaret Hospital. In 1966 these registries reported 5,806 new cases, and as nearly 40 per cent of the 8,582 new patients registered at the treatment centers had surgical treatment in the course of their disease, a considerable number of case reports of patients treated by surgery or medical means are now available for study.

Combined clinical conferences of the radiotherapists, pathologists, and surgical and medical consultants of the Princess Margaret Hospital and regional clinics have been held annually since 1954. Table III indicates the features of the conferences.

Naturally the number of cases for review has increased greatly in recent years because registrations at the centers have increased by 60 per cent in the last 15 years, and the programs have broadened to consider all phases of the tumors under study and all methods of treatment. Guest speakers from this country, Great Britain and other parts of Canada are adding their experiences to the programs which have a distinct educational value to the local physicians and surgeons who are invited to attend. Probably the most valuable feature, however, is the effect on the permanent staffs of the Princess Margaret Hospital and the regional centers as they review the results which each can produce with variations in techniques and procedures.

It is essential that any program of centralized cancer services should have the authority of the Government, the approval of the medical profession and the cooperation of voluntary agencies supported by the public. Our experience has shown that centralized radiotherapy is essential to a high standard of treatment and is the only means of providing trained personnel to ensure the future of this specialty. This applies not only to radiotherapists but also to highly trained radiation technicians, the importance of whose function is steadily increasing. The proper recognition of departments of radiotherapy in the medical schools* is necessary in order to present to undergraduate students and residents the importance of radiotherapy in the treatment of cancer. Hormone and chemotherapy have become so closely related to radiotherapy that medical services in the centers have become an established necessity. However, this does not alter the fact that all first-class general hospitals should be equipped and prepared to treat and investigate the large percentage of malignant lesions which now come within the sphere of medical care. The centralization of surgical services is open to much stronger arguments, both pro and con. The value of the work of surgical departments in certain well known cancer hospitals is beyond question, but many have some doubt as to the wisdom of isolating surgeons and confining them to one field of endeavor. The alternative of providing consultants from clinical departments, with major surgical treatment being undertaken in the highly organized operating rooms of large general hospitals by specially chosen members of the staffs, has some advantage in that it does not dissociate them from a wider field of surgical treatment. Another phase of this question is the need to gain the ap-

* There will be 5 medical schools in Ontario by 1969 with the addition of Ottawa (1951) and McMaster University, Hamilton (1969).

proval and support of organized medicine in accepting a program which may exclude well trained and competent surgeons from performing what has been recognized as very valuable service in good general hospitals not directly associated with the central organization. With a well organized central control it is easier to co-operate with the Cancer Society, which has been very generous in providing funds for special building projects and which, in Ontario, has become responsible for public educational campaigns and the provision of many welfare services to cancer patients. It has taken time to develop the program in Ontario which is the product of many minds, and it has always been necessary to justify the expenditures of money which has not always been easy to obtain. Finally, changes have been made and undoubtedly will be made from time to time to accommodate changing circumstances. Our experience indicates the need of flexibility and that the success of centralization may depend on the services provided beyond the highly organized centers.

Since this Lecture was prepared the author has had the experience of attending the International Symposium on Radiation Therapy at the Memorial Sloan-Kettering Cancer Center, and it appears that a new concept of centralized cancer services may have to be considered.

Up to now, success in treating cancer had depended on early recognition of the disease, and surgeons, radiotherapists and physicians applying their personal skills in undertaking its treatment. This is still true today. But at the same time, the radiotherapist, becoming ever more a scientist, but still no less a physician, dominant because of the great advances of this scientific age, drawn into great institutions receiving almost limitless financial support, is facing his most serious problem, namely the recruiting of his own specialty, and the physicists and technicians who make his work possible. Computer control to extend treatment from a major center to other hospitals is only a very partial answer and cannot replace the human factor in meeting the needs of the individual patient.

Circumstances always alter cases and it is very doubtful if any one plan of centralization will satisfy every situation. The most we claim, therefore, for the program which has evolved in Ontario, is that for the time being it seems to be reasonably satisfactory.

207 Balmoral Avenue
Toronto 5, Ontario
Canada

THE VALUE OF RADIOTHERAPY IN THE MANAGEMENT OF ESOPHAGEAL CANCER*

By J. G. PEARSON
EDINBURGH, SCOTLAND

THIS report is based on a series of 1,870 patients with primary carcinoma of the esophagus seen in the radiotherapy or surgical departments in Edinburgh. In South East Scotland, the region around Edinburgh, there is only one radiotherapy center and one group of thoracic surgeons serving a population of one and one-third million persons. During the 12 years, 1956 to 1967, we have seen 805 patients, nearly all the cases of esophageal cancer occurring in this population. This series is of patients with squamous cell carcinomas. The adenocarcinomas in the esophagus from this population have been excluded as a mainly surgical problem and they are reported elsewhere.[7,8,9]

PATTERN OF MANAGEMENT, 1931 TO 1967

From 1931 to 1947 there were 618 patients seen. Of these, 154 (25 per cent) were treated radically by radiotherapy, 27 (4 per cent) were treated by operation and 437 (71 per cent) received only palliative or no treatment (Fig. 1). Radiotherapy was the only effective method of treatment. Five irradiated patients (1 per cent of all patients) who had cervical esophageal cancers survived 5 or more years. None of the patients with thoracic esophageal cancer survived free from tumor for 5 or more years but 9 per cent of them gained significant palliation and survived from 1 to 2 years.[17]

From 1948 to 1955 there were 447 patients. During this period a new factor was introduced which resulted in a radical alteration in the pattern of management. As a consequence of the development of thoracic surgery as a separate specialty, successful resections of thoracic esophageal cancer were carried out for the first time in Edinburgh, and some of these patients are alive to this day.[7,8,9] Because of the relative success of surgery during this period, the radical irradiation of thoracic esophageal cancer was abandoned and radiotherapy was reserved for the treatment of cervical esophageal cancer, where it continued to achieve success, and for the palliative treatment of inoperable cases. Of the 447 patients seen during this period 17 (4 per cent) with cervical esophageal cancers were irradiated radically, 189 (42 per cent) were treated by operation and 241 (54 per cent) received only palliative or no treatment (Fig. 1). Thirty-two (7 per cent of all patients) survived 5 years.

From 1956 to 1962 there were 429 patients. During this period other new factors were introduced: first a four million volt linear accelerator was brought into use in Edinburgh; and second, by 1956 it was possible to use in the planning of radiation treatment the increasingly rich store of information available as a result of the surgical experience. It was possible at that time to predict more precisely than in 1947 the likelihood of any particular esophageal cancer being fully included within any one defined volume of tissue. Therefore, the time was thought to be favorable to investigate again the value of radiation therapy in the treatment of thoracic as well as cervical esophageal cancer. In view of our disappointing experience with thoracic esophageal cancer in the days of orthovoltage therapy, at first only a few clearly inoperable patients were irradiated, but as more and more were found to have gained striking benefit, and their survival pattern was found to be better than survival after surgery, we increasingly preferred irradiation to surgery. Of the 429 patients seen during this period 99 (23 per cent) were irradiated

* Presented at the Fiftieth Annual Meeting of the American Radium Society, Miami Beach, Florida, April 7–11, 1968.
From the Department of Radiotherapy, The Royal Infirmary, Edinburgh, Scotland.

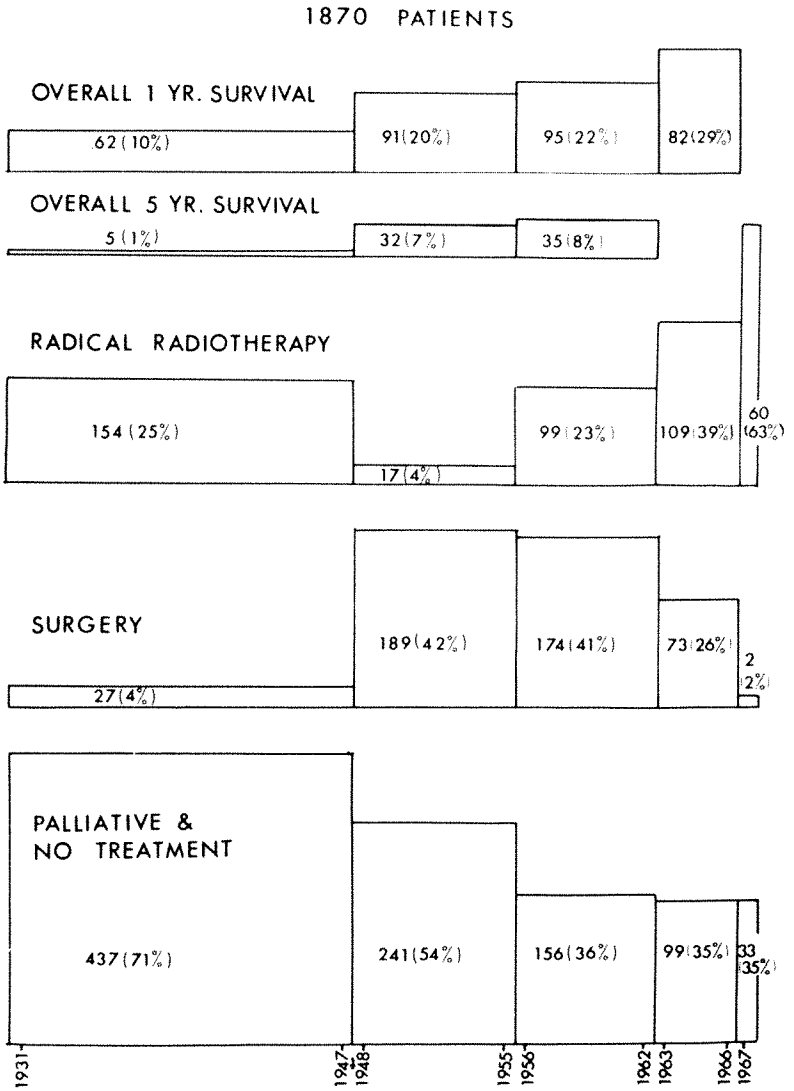


FIG. 1. One thousand, eight hundred and seventy patients with carcinoma of the esophagus (including all levels but excluding adenocarcinomas) divided according to 5 periods of years from 1931 to 1967 and the 3 main methods of management: radical radiotherapy; surgery; and palliative or no treatment. The numbers of 5 year and 1 year survivors are indicated along the top two lines. The percentages shown are out of the total number of patients which occur in each period and the height of each block is in proportion to the percentage.

radically, 174 (41 per cent) were treated by operation and 156 (36 per cent) received only palliative or no treatment. Nearly two-thirds of all patients seen were offered treatment with some chance of cure as compared with one-quarter from 1931 to 1947 and less than one-half from 1948 to 1955. Although the radically irradiated patients had no known advantages other than their method of treatment, their 5 year survival rate is 20 per cent as compared with 9 per cent for the patients treated by operation during these years. The over-all 5 year survival rate of the 429 patients seen during this period is 8 per cent.

From 1963 to 1966 there were 281 patients. During this period, as during the period 1956 to 1962, nearly two-thirds of all patients seen have been offered potentially curative treatment, but a higher proportion

has been treated by irradiation than by operation (Fig. 1). The change-over from surgery to irradiation has occurred earlier for patients with tumors in the upper half of the thoracic esophagus where the difficulties are strikingly greater for the surgeon but apparently no greater for the radiotherapist. Of the 281 patients seen during this period 109 (39 per cent) were irradiated radically, 73 (26 per cent, including 60 patients with tumors in the lower half of the thoracic esophagus) were treated by operation and 99 (35 per cent) received only palliative or no treatment. The over-all survival pattern over intervals of less than 5 years is slightly more favorable than for the period 1956 to 1962 and this gives a reasonable expectation of a further small increase in the 5 year survival rate.

In 1967, there were 95 patients. Sixty (63 per cent) were irradiated radically, 2 (2 per cent) with tumors at the lower end of the esophagus, for which histology was not available prior to operation, were treated by operation, and 33 (35 per cent) received only palliative or no treatment. The current Edinburgh policy is to offer radiation therapy in preference to operation as the initial treatment for all potentially curable patients with squamous cell carcinoma of the esophagus, whatever the level.

DISCUSSION OF THE PATTERN OF MANAGEMENT

In a situation where it has not been possible to compare the value of two methods of treatment by a controlled trial, wherein the patients are allocated randomly to one or another method, the assessment of the comparability of the two groups of patients to which the two treatment methods have been applied is of critical importance, but at best it is an inexact measurement. The age and sex of the patient may be accurately recorded and reasonable accuracy may be achieved in defining the site of the tumor, but as to its extent, including any lymphatic or blood borne spread, each estimate is attended by great inaccuracy. This is particularly disturbing in view of the necessary preoccupation of either the radiotherapist or the surgeon with the accurate measurement of the true limits of the tumor. There are other factors even less amenable to measurement and there may, indeed, be unknown factors affecting the patient's survival present unequally in the two treatment groups. One of the great attractions of a random trial is that even the unknown factors are likely to be equally distributed between two groups of patients.

A more detailed analysis of the comparability of the irradiated and the operated groups of patients is made in a previous paper[17] and the distributions of age, sex, tumor site, tumor extent and completeness of histologic confirmation among the additional patients seen in the years 1965, 1966 and 1967 follow closely the 1956–1964 pattern and present no features tending to invalidate the conclusion that the most probable explanation of the higher survival rate of the irradiated group is that radical megavoltage irradiation is a more suitable method of treatment than surgery for patients with squamous cell or undifferentiated carcinoma of the esophagus. It is quite possible that there is a smaller group of patients submerged in the above analysis for which this conclusion is not valid and in this connection the results will be analyzed according to the level of the tumor.

Owing to the difficulty of judging the comparability of the two groups there remains an inescapable element of uncertainty. Confirmatory work is necessary. The most positive step to provide confirmation that it seemed ethical to take in Edinburgh was to irradiate rather than operate. This is now being done. In the context of the well-defined and stable population in the Edinburgh region, exclusively served by a single regional radiotherapy service, this complete change from surgical to radiotherapeutic management within a period of 6 years constitutes a clinical investigation probably only slightly inferior to a random trial in investigating the relative value of the two methods of treatment.

To the worker in another center, consid-

ering to what extent this work is applicable in his environment, the question must arise as to the quality of the surgery with which radiotherapy is being compared. The surgical work in Edinburgh from 1948 to 1962 has resulted in 41 patients surviving 5 or more years, 11 of these 41 having had tumors in the surgically difficult upper half of the thoracic esophagus. It should also be noted that while the 5 year survival rate is only 11 per cent of all patients subjected to operation, it is 13 per cent of those actually resected, 20 per cent of those still alive 1 month after resection and 23 per cent if patients over 75 years of age are excluded. It is also important to note that these results have been obtained during a period when over 40 per cent of all patients seen with esophageal cancer out of a defined general population have been subjected to surgery in an all-out effort to ensure that no patient, even if he had only a small prospect of doing well, was denied the chance of cure. I know of no better surgical achievement in such a context.

PATTERN OF SURVIVAL SINCE 1956
RADIOTHERAPY AND SURGERY

Neither radiotherapy nor surgery appears to be a satisfactory treatment for patients with esophageal cancer as they present to us in Edinburgh. More than one-third of the patients already have evidence of blood borne metastases, lymphatic spread remote from the primary tumor, esophagotracheal fistula or a primary tumor demonstrably more than 10 cm. in extent, and for these reasons they are excluded from an attempt at curative treatment. Such patients have been treated only palliatively or, in some very advanced cases, given no treatment at all. Ninety-three per cent of them die within a year and none has survived 5 years.[17]

Of the remaining two-thirds with less grossly advanced demonstrable cancer some have been irradiated and some operated. Only 20 per cent of the irradiated patients and 9 per cent of the operated patients are alive 5 years later. (Of the 363 patients

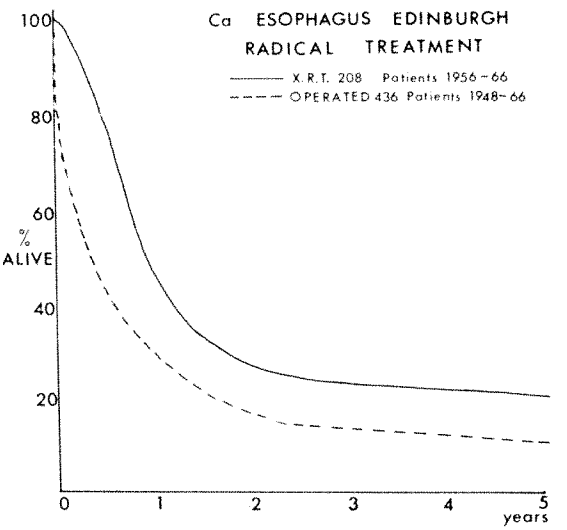


FIG. 2. The survival curves of 208 patients radically irradiated from 1956 to 1966 and 436 patients subjected to operation (whether resection was possible or not) from 1948 to 1966. Ninety-nine of the irradiated patients and 363 of the operated patients were treated more than 5 years ago. X. R. T. = x-ray treatment.

operated from 1948 to 1962, 11 per cent were alive 5 years later.) Both radiotherapy and surgery make only a localized attack on what is often a generalized disease. Even locally, both often fail. The effect of radiotherapy in eliminating tumor may occasionally be extended a little further anteroposteriorly and laterally than the block of tissue resected, but the length of the esophagus irradiated is not always longer than the length which can be resected. We do not frequently irradiate more than a 15 cm. length of esophagus (and rarely less than a 13 cm. length). After either radiotherapy or surgery, recurrence has been seen in tissue more than 5 cm. beyond the naked eye limits of the primary tumor, and after irradiation local recurrence in the primary site or even failure of the tumor to disappear is all too common.

All that appears to be established by the Edinburgh series is that radiotherapy less frequently causes the early death of the patient than does surgery (Fig. 2). The high local recurrence rate following irradiation, even higher than that following surgery,

contributes in part to the slope of the survival curve for irradiated patients being steeper than that for operated patients during the interval from 3 months to 2 years after treatment. However, this highly unfavorable feature is somewhat less disastrous than the strong tendency of operative treatment to bring about the early death of many patients. Accordingly, 2 years after treatment, 27 per cent of the irradiated patients compared with 18 per cent of the operated patients are still alive. Thereafter, the two survival curves run parallel, leading to a 5 year survival rate of 20 per cent for the irradiated patients and 11 per cent for those treated by operation. It is of interest that the mean age of the 2 year survivors in the irradiated series is 65.7 years compared with 62.6 years in the surgical series, but the late fall-off in survival after 2 years is no greater for the irradiated than it is for the operated patients.

THE LEVEL OF THE ESOPHAGEAL CANCER

The level of the tumor in the esophagus has an important bearing on the survival pattern, especially for the operated patients. In Figure 3 the 5 year survival rates of 363 patients treated by operation from 1948 to 1962 and 99 patients treated by radical radiotherapy from 1956 to 1962 are compared level by level.

In the cervical esophagus, 31 patients were irradiated radically. Seven (23 per cent) survived 5 or more years. Each has a normal voice. Fourteen patients were treated by operation. Three (21 per cent) survived 5 or more years. Each has no voice or a poor substitute. The mean size of demonstrable tumor in the irradiated patients was 6.1 cm., but in those treated by operation it was 5.1 cm. The numbers are small but remembering the appreciable difference in tumor extent it seems probable that comparable patients stand at least as good a chance if irradiated. The most important difference is that the irradiated patient retains his larynx.

In the upper half of the thoracic esophagus 39 patients were irradiated radically. Eight (20 per cent) survived 5 years. One hundred and twenty-eight patients were treated by operation. Eleven (9 per cent) survived 5 years. Although over-all the incidence of carcinoma in the upper half of the thoracic esophagus is nearly equal to the incidence in the lower half, in the surgical series there is only a little more than one-half as many patients with tumors in the upper half as compared with the lower half. In the radiotherapy series there are more patients with tumors in the upper half than in the lower half of the thoracic esophagus. This is a result of the need for stricter selection for surgery in the upper half of the thorax because of the higher operative mortality and the smaller chance of being able to resect the whole of the tumor. In fact, in the upper half of the thorax, the change-over from surgical to radiotherapeutic management has been almost complete since 1960 and, although the numbers

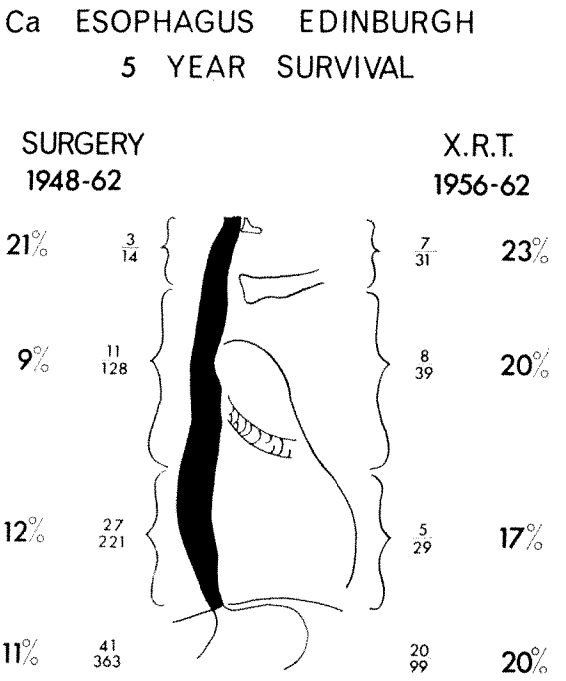


FIG. 3. The 5 year survival rates of 363 patients subjected to operation from 1948 to 1962 and 99 patients radically irradiated from 1956 to 1962 are shown according to three levels: cervical esophagus; upper half of thoracic esophagus; and lower half of thoracic esophagus. X.R.T. = x-ray treatment.

irradiated at this level alone are still too small for complete confidence, the 20 per cent 5 year survival rate may be taken as a fair indication of what to expect when irradiation is used as the mainstay of treatment at this level.

In the lower half of the thoracic esophagus 29 patients were irradiated radically. Five (17 per cent) survived 5 years. Two hundred and twenty-one patients were treated by operation. Twenty-seven (12 per cent) survived 5 years. At this level the operative mortality is not so high and the surgical results are consistently better than in the upper half of the thorax, even though more than half of all patients seen with tumors in the lower half of the thoracic esophagus have been subjected to operation. The results of irradiation at this level are less clearly established. So far only 29 patients have been irradiated more than 5 years ago. They are only a small selection of patients with tumors at this level and they may be far from representative. The 5 year survival rate may turn out to be appreciably higher, or lower, than 17 per cent in the light of further experience. Since February, 1966, the Edinburgh practice has been to treat by irradiation, rather than operation, all patients with squamous cell carcinoma of the esophagus, including those with tumors invading the stomach and including fit young patients who would be likely to do well with surgery. A clearer picture should soon emerge of the value of irradiating tumors at the lower end of the esophagus.

QUALITY OF LIFE FOLLOWING IRRADIATION

When assessing the value of a method of treatment, the length of survived life receives the most attention because of its fundamental importance, the objective nature of the measurement and the possibility of precise recording. It is the most suitable criterion for comparison between different series. Nevertheless, the quality of the survived life, while less amenable to measurement, is of immense importance to the patient.

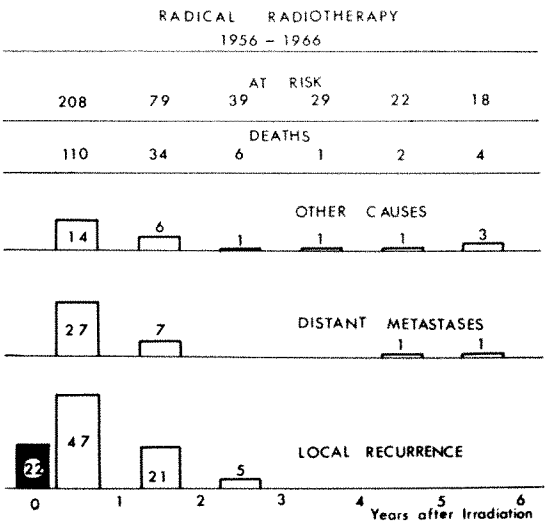


FIG. 4. Of 208 patients with squamous cell carcinoma of the esophagus radically irradiated from 1956 to 1966, 157 had died by the end of 1967. The annual number of deaths in the first to the sixth years after treatment is shown according to three causes: local recurrence (and initial failure); distant metastases; and other causes. The total number of deaths in each yearly interval and the corresponding number of patients at risk are shown on the top two lines.

MODE OF DEATH

Eighty per cent of the radically irradiated patients die within 5 years of treatment. Clearly they have received only limited benefit. In Figure 4 are shown the deaths that have occurred year by year following the radical irradiation of 208 patients between 1956 and 1966. They are divided into three categories. On the bottom line are shown the deaths which occurred mainly due to local recurrence, whether or not other factors such as distant metastases were thought to contribute. On the second line are deaths mainly due to distant metastases. On the third line deaths due to other causes. Twenty-two deaths, which occurred within 3 months of treatment, have been attributed to initial failure in management and are shown on the bottom line.

Of the 135 patients dying from causes other than initial failure of treatment, 73 (slightly more than one-half) have died from local recurrence of carcinoma in the esophagus. So far, all the local recurrences

have occurred within 3 years of treatment. One-half of the local recurrences occurred within 6 months of treatment. Nearly one-half of the patients who eventually died from a local recurrence had experienced sufficient relief from dysphagia to take a normal diet for a worthwhile period. Eight of the patients dying from a local recurrence were recognized to have a fistula to the tracheobronchial tree. In 7 other cases a massive hemorrhage was the terminal event.

Most of the early patients in the radically irradiated series had been classed as inoperable by the time it had been recognized that a local recurrence had developed. In more recent years, a local recurrence has developed in some patients who were technically operable before irradiation, and 19 of these patients were still operable by the time a local recurrence was recognized. So far no patient's survival has been extended by more than 15 months by means of resection following irradiation failure, but now that all the technically operable patients are being irradiated, some of the radiation failures should not present such a hopeless prospect for the surgeon, and in the future we may hope for a small contribution to the over-all salvage rate by surgery for radiation failures. The diagnosis of locally recurrent tumor after irradiation is difficult. In some cases, following elimination of all tumor, there may be quite a gross distortion of the lumen and loss of elasticity of the esophageal wall impossible to distinguish roentgenographically from tumor (Fig. 5). In other cases an ulcerated carcinoma may heal over following irradiation, but a local recurrence may develop deep in the esophageal wall under intact mucosa and inaccessible to endoscopic biopsy. Three patients subjected to resection of the esophagus for what was believed to be locally recurrent tumor had no tumor detectable on histologic examination of the resected specimen. Two of these 3 patients died as a result of the operation.

For the 54 patients dying from locally recurrent tumor for whom an attempted resection seemed to offer no hope of cure, intubation made possible the swallowing of a liquid diet for a few extra weeks in some cases. For a few patients intubation or an attempt to intubate abbreviated life, which for most of them had already lost its savor. The establishment of a permanent gastrostomy was carefully avoided in the case of patients whose esophageal cancers were incurable.

Thirty-six patients died from distant metastases, especially in the liver or lungs, and, with two exceptions, all within 2 years of treatment (Fig. 4). One patient died from liver metastases in the fifth year, and another from widespread intra-abdominal metastases in the sixth year. Most of these 36 patients enjoyed a normal diet from a few weeks after irradiation up to their terminal illness.

Twenty-six patients died of causes not directly related to the esophageal cancer. Their mean age when first treated (71 years) was, not surprisingly, higher than for the series as a whole (67 years). The incidence of deaths from other causes, as a fraction of the number of patients at risk, tends to rise year by year after treatment. Nearly all these patients had enjoyed a normal diet from a few weeks after treatment until their terminal illness.

LIFE OF THE 5 YEAR SURVIVORS

Each of the 20 patients who so far (December 31, 1967) have lived 5 or more years following irradiation has a normal voice and a normal stomach and has regained a normal or excessive weight. Those under retirement age are working. Seventeen out of the 20 take a normal diet. One of the 3 not taking a normal diet by the fifth anniversary of treatment had a fibrous stricture due to a peptic ulcer which antedated her carcinoma by 13 years and had been treated by bougienage on 3 occasions before the development of the carcinoma. The squamous cell carcinoma 7 cm. higher up her esophagus had been healed by irradiation without any stricture at that level. Another patient has a fibrous stricture at the site of healing of a large midcervical esophageal cancer irradiated in 1957. She can drink and she can

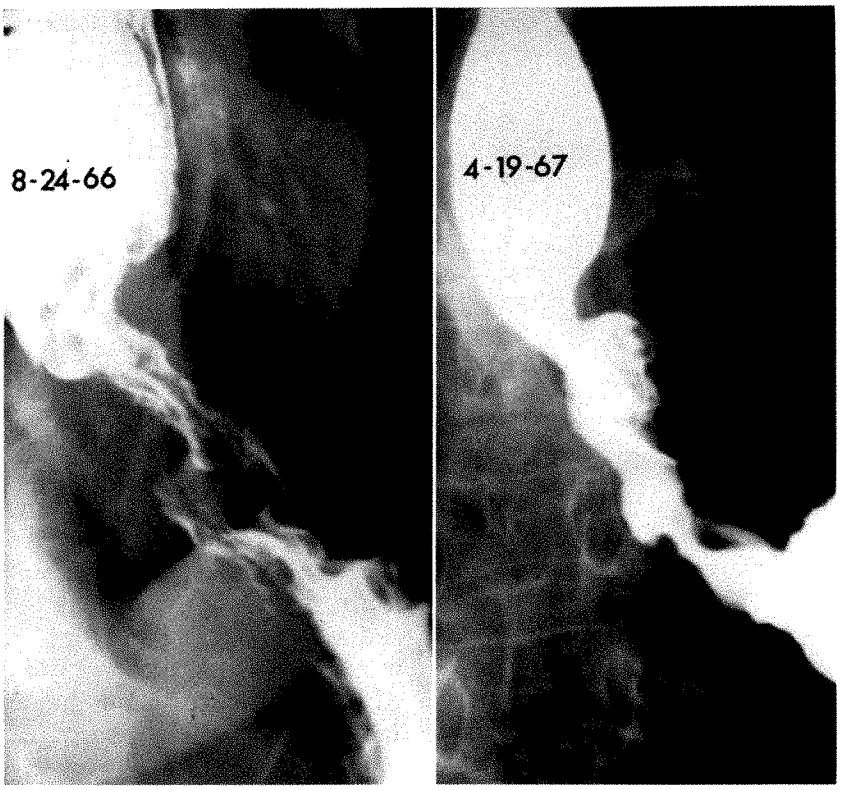


FIG. 5. An exuberant type of well differentiated squamous cell carcinoma at the lower end of the esophagus of a 63 year old woman irradiated in August–September, 1966, but still presenting gross residual distortion of the esophageal lumen in April, 1967. The patient was clinically well and had regained weight. The biopsies were negative but the roentgenographic appearance so strongly suggested the presence of recurrent carcinoma that an esophagogastrectomy was performed in May, 1967. In the resected specimen a 6 cm. length at the lower end of the esophagus presented polypoidal excrescences and ulceration within a rigid tube, but histologic examination showed radiation changes with sclerosis and ulceration with no evidence of tumor.

swallow her saliva but feeds herself by a gastrostomy. She refuses surgery for the stricture. The third 5 year survivor whose swallowing was never restored to normal was a 78 year old man with a squamous cell carcinoma 32 cm. from the upper alveolus which was irradiated in 1959, leaving a short stricture (Fig. 6). During the first 2 years following irradiation the stricture was dilated with bougies on 8 occasions, with little permanent benefit. Thereafter, the patient refused further procedures, preferring to subsist on a semi-liquid diet. When last seen, 7 years after irradiation, he was maintaining his weight and leading a normal life for an 85 year old man.

Of the 17 euphagic 5 year survivors, 9 have required bougienage. Four patients each required bougienage on only 1 occasion and 5 patients required repeated bougienage. Two of the patients who required repeated bougienage were finally able to maintain a satisfactory aperture through the esophagus by the daily use of a mercury bougie. One of these patients had the most troublesome stricture in this series. She was referred to us in 1961 when she was 59 years old with a squamous cell carcinoma at 33 cm. from the upper alveolus (Fig. 7). Ten months after irradiation there was still a long and quite narrow stricture at the site of healing of the carcinoma. Repeated bougienage was required and finally the use of a mercury bougie up to the end of the third post-treatment year. Thereafter she has taken a normal diet without further instrumen-

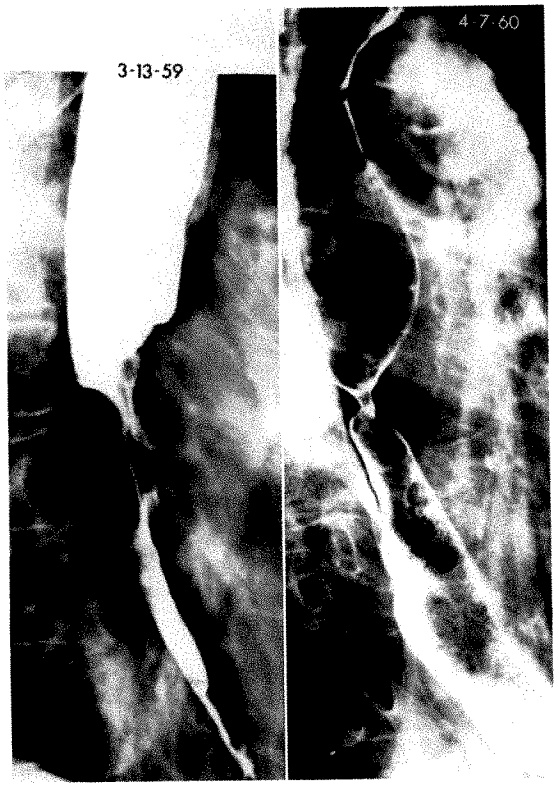


FIG. 6. A squamous cell esophageal carcinoma in a 78 year old man irradiated in March, 1959 leaving a short stricture as demonstrated above in April, 1960. He was treated by the passage of bougies until March, 1961, since when he has maintained his weight on a semi-liquid diet.

tation. She leads a normal life and is a little overweight.

An example of the four 5 year survivors who required bougienage on only 1 occasion was a 69 year old man with squamous cell carcinoma 31 cm. from the upper alveolus. The pretreatment roentgenographic appearance of the tumor on November 10, 1962 is shown in Figure 8*A*. When he was referred to the radiotherapy department 2 weeks later the carcinoma completely obstructed the esophagus. His nutrition was maintained solely by the intravenous route during the first 3 weeks and by a nasogastric tube during the fourth and last week of radiotherapy. At the end of the course of radiotherapy on December 28, 1962 there was still a narrow stricture but the tumor was shrinking in the usual way (Fig. 8*B*). Two months later, on February 21, 1963, the extensively ulcerated carcinoma had healed except for a small area of mucosa on the posterior aspect of the short residual stricture (Fig. 8*C*). Until mucosal healing is complete there is an element of spasm in the stricture. Thereafter, on 1 occasion only, bougies were passed gently to dilate the stricture. He rapidly regained weight and returned to a normal life which he was still enjoying when last seen in January, 1968. A roentgenogram made on December 3, 1964 (Fig. 8*D*) shows loss of elasticity of the esophagus over a short segment corresponding to the center of the original carcinoma. This residual abnormality is common as a late finding and is quite compatible with a perfect clinical result. Figure 9 is a photograph of the patient 3 years after irradiation, 56 pounds (25 kg.) heavier. Also shown is a skin graft used to repair an area of radiation necrosis on the dorsum of the left wrist induced by a roentgenographic in-

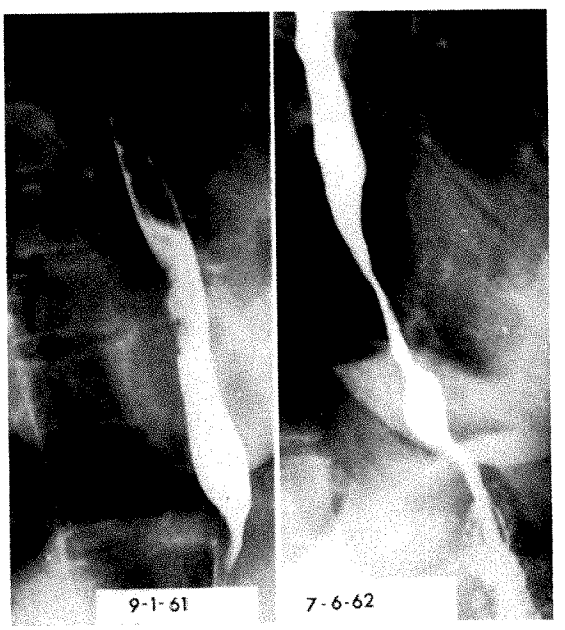


FIG. 7. A squamous cell esophageal carcinoma in a 59 year old woman irradiated in September, 1961 leaving a long stricture as demonstrated above in July, 1962. She was treated by the passage of bougies until September, 1964, since when she has taken a normal diet without further instrumentation.

vestigation using soft x-rays from an old gas tube following an injury in 1919. It gives pleasure to record how radiology has now atoned for an injury done half a century ago.

Eight of the 17 euphagic 5 year survivors presented no difficulty. One was a 56 year old woman with a bulky, 9 cm. long squamous cell carcinoma at the level of the aortic arch. She had treatment as an outpatient and continued to look after her house and family throughout the 4 week course of radiotherapy. With the exception of rather

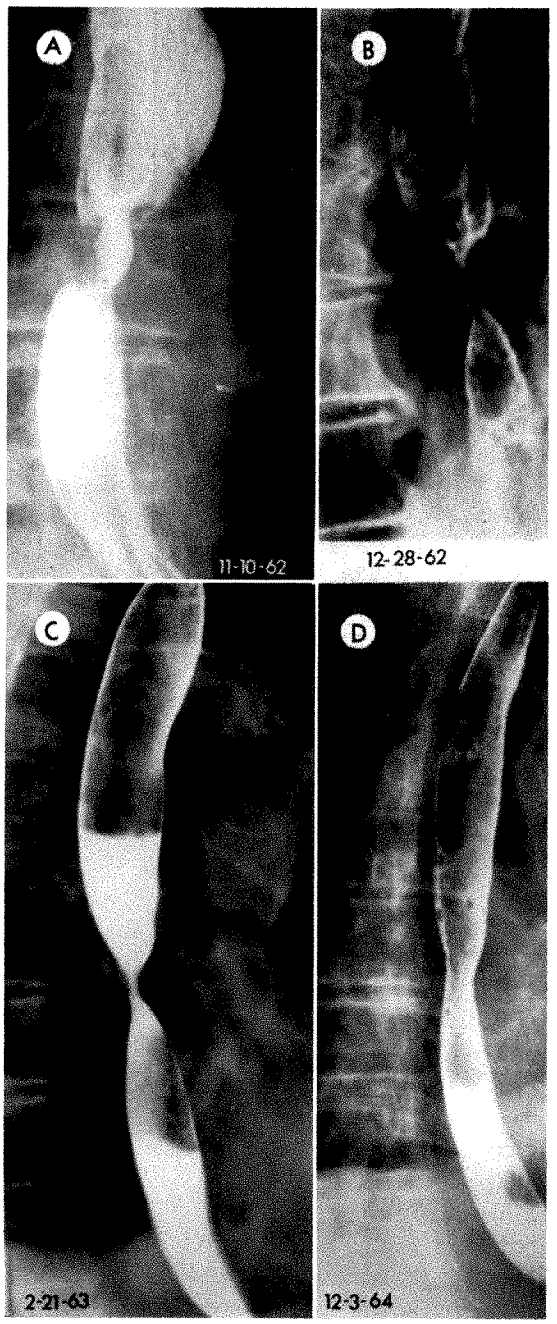


FIG. 8. (*A*) A squamous cell esophageal carcinoma in a 69 year old man irradiated in December, 1962 while dysphagia was complete. (*B*) At the end of the course of irradiation a narrow lumen appeared, making possible the passage of a nasogastric tube followed a week later by the re-starting of oral fluids. (*C*) On February 21, 1963, 2 months after irradiation, there was still a small ulcer on the posterior aspect of the short residual stricture. Thereafter, one gentle dilatation was carried out. (*D*) In December, 1964 the only residual abnormality was slight loss of elasticity of the esophageal wall over a short segment corresponding to the center of the original carcinoma.

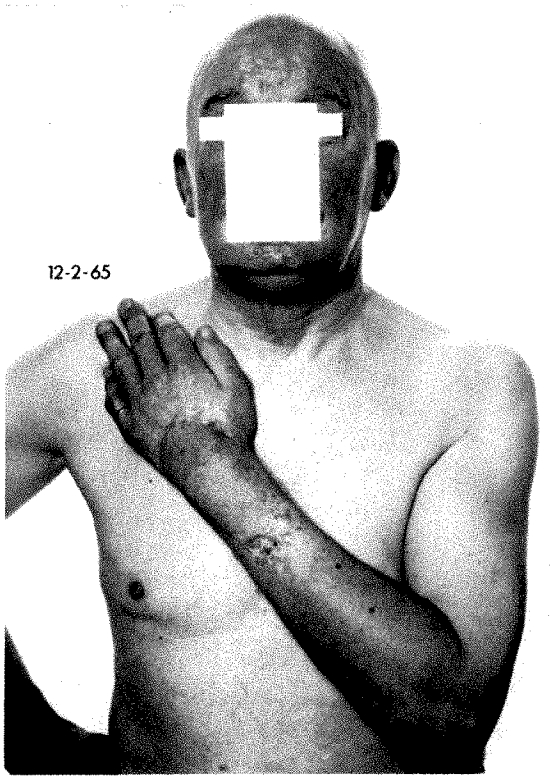


FIG. 9. By December, 1965 the patient whose esophagus is illustrated in Figure 8, *A–D* had put on 56 pounds in weight. He swallowed normally. In 1919 he had suffered a radiation injury to the skin on the back of the left wrist, which has since been repaired by a skin graft.

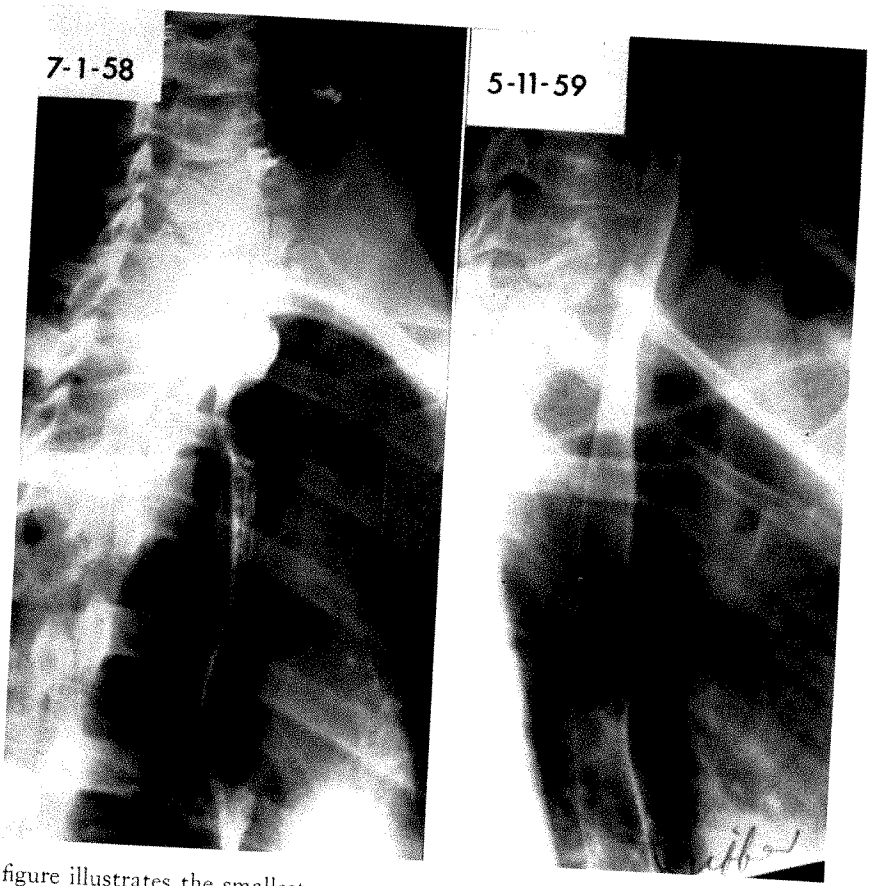


FIG. 10. This figure illustrates the smallest squamous cell carcinoma treated by irradiation since 1956. It arises from one wall of the lower cervical esophagus of a 50 year old man. The carcinoma was irradiated in July, 1958. A normal esophagogram, illustrated above, was obtained in May, 1959 and the patient remained symptom free when he was last seen in July, 1967.

gross obesity, there have been no complications. Generally, as in other sites, it is the smaller tumors which give the least trouble. The smallest tumor occurring in the irradiated series was found confined to one wall of the lower cervical esophagus in a 50 year old laborer (Fig. 10). It was irradiated in 1958 and, predictably, the patient has been euphagic and working normally ever since.

TECHNIQUE

When the cure of a cancer patient is to be attempted, whether by radiotherapy or surgery, the first vital task is to estimate with the greatest possible accuracy the local extent of the tumor, the extent of lymphatic spread and the likelihood of distant metastases. The difficulties are only too well known. The meager evidence assembled by clinical, roentgenographic, and endoscopic examinations and the histologic examination of biopsy material falls very far short of the complete picture it would be desirable to have of the distribution of all viable malignant cells throughout the body. In 35 per cent of the patients in the Edinburgh series it was possible to demonstrate the presence of a tumor of such an extent as to make any attempt at cure unwise. Of the remaining 65 per cent, 76 per cent of those with tumors in the upper half of the thoracic esophagus subjected to thoracolaparotomy had tumor dissemination demonstrated in the course of the operation.[8] The extent of tumor in those patients not subjected to thoracolaparotomy but treated by irradiation is not likely to have been any

less. In the absence of certain knowledge of such spread, cure was attempted. The assessment of the probable extent of spread beyond the demonstrable limits of the tumor is so much a matter of inference based on past experience of the incidence of various patterns of failure due to local or distant spread that it is difficult to lay down any simple plan adequate, say, for any occasional practitioner in this field. The first requirement for success in the management of the cancer patient is an intimate aquaintance with the natural history of the disease. This would hardly need stating were it not for the very real inadequacy of information so far available about the patterns of variation which may be induced in the natural history of esophageal cancer by treatment. The student will readily find descriptions of rapidly fatal disease and the subsequent findings at autopsy, but only in the last 20 years has much information become available about the incidence of marginal recurrence, remote lymphatic spread and distant metastases following local eradication of thoracic esophageal cancer.[1–5, 7–14,18–20,25]

Armed with this knowledge and especially after considerable experience of applying it to the management of esophageal cancer, the therapist may assess the probability of any one patient's tumor being fully included within a particular target volume, and he may balance that probability against the probabilities of any one radiation dose given to that volume achieving local control of the cancer, or doing intolerable damage to the patient.

The Edinburgh practice has been to vary the radiation dose over a very small range and to vary the target volume over a larger range than the dose, but a smaller range than the sizes of demonstrable tumor. Thus a large tumor will be allowed a smaller margin than a small one, the need to keep the volume small enough to tolerate an adequate dose being held to take precedence over the need to achieve any one level of probability of including all tumor.[17] The doses used range closely around 5,000 rads given in 20 equal fractions in an over-all time of 28 days. The most frequently treated volume is a somewhat ellipsoidal solid of rotation of a 14×7 cm. rectangle with rounded off corners, but the shape, size and positioning of the treated volume is highly individualized. The patient is treated lying in the supine and prone positions. The supine position alone will be used when a linear accelerator with 360° rotation becomes available. For the thoracic esophagus a single anterior and two posterolateral fields are used, the axis of the target cylinder usually lying at a small angle to both the sagittal and coronal planes so as best to include the suspect tissues and avoid the spinal cord. For thoracocervical tumors, two anterolateral double wedge filtered fields are used. An individual reduced absorption allowance is made for the amount of lung intervening in each field. Careful attention to detail is used in treatment planning, the medical time devoted to the task averaging 3 hours. Similar to the experience of Leborgne *et al.*,[6] there have been 3 patients who have developed partial necrosis of one or more vertebral bodies, the anterior portions of which are always included in the fully irradiated volume. There has been no case of spinal cord damage. Since the introduction of this technique in 1956 a three dimensional check has been made on spinal cord dose in every case. In no case has the spinal cord been included in the fully treated volume and in most patients the spinal cord has received substantially less than 4,000 rads in 20 fractions in 28 days over-all. Lung fibrosis has been very minor in degree and has rarely given rise to symptoms.

DISCUSSION OF TREATMENT

Veraguth[23] reported the local persistence of tumor in 4 patients even following doses between 7,750 r and 10,000 r in 5 to 6 weeks using 31 mev. electrons. Seaman and Ackerman,[21] in a study of the effect of radiation on the esophagus, stated that doses higher than 6,000 r in 6 weeks may give serious sequelae. Smithers,[22] after a very searching

study of the disease, states that "doses of much more than 1,000 r to the tumour each week for six weeks or longer, carry a real risk of damage which increases markedly with the size of the volume irradiated." The variability in the response to radiation is greater for tumor than for normal tissue. It is probable that a moderate increase in dose above 5,000 rads in 20 fractions in 4 weeks would achieve only a small reduction in the local recurrence rate at the expense of quite a large incidence of complications. As a result of a study of the surgical experience in Edinburgh,[7,8,9] it seems unlikely that more than 30 per cent of the patients at present offered radical treatment would survive 5 years, even if complete eradication of the primary tumor was achieved in every case. It must be remembered that some (an unknown percentage) of the patients who suffer a local recurrence of tumor already have distant metastases before treatment is started.

In Edinburgh there is no intention immediately to respond with a higher dose to meet the recognized high local recurrence rate associated with the technique described. To raise the dose given to such large volumes in this region of the body in frail old patients may well do more harm than good. It might add to the present difficulties of the radiotherapy of the disease a significant treatment mortality, the present absence of which is one of the major advantages of radiotherapy over surgery.

The aim is to determine the best over-all pattern of management for esophageal cancer, at all stages of advancement, as it presents in our community. Radiotherapy alone, or surgery alone, is not necessarily the best answer. Nakayama[15] and co-workers[15,16] have recommended a sublethal dose of radiation followed by early resection, but to subject every potentially curable patient to a combination of radiotherapy and surgery may be to inflict increased risks without commensurate reward. The addition of chemotherapy is open to a similar criticism. Each is an additional assault on a generally frail cachectic old patient. The maximum preservation of both local tissue response and the immunologic integrity of the patient as a whole may yet prove to be important aims. Even when the disease appears to be localized, wide dissemination may be present. Accordingly, in agreement with the practice recommended by Watson,[24] having given potentially curative irradiation, no further assault is made on the patient unless it is established that the initial treatment has failed.

SUMMARY

The surgical management of carcinoma of the cervical and upper thoracic esophagus is not entirely satisfactory. Unless the surgeon is so highly selective that his method of treatment hardly amounts to a serious contribution to the over-all management of the disease, the operative mortality is high. For a patient to die as a result of the method of treatment is a tragedy, tolerable only if balanced by a very appreciable expectation of cure. No present available method of treatment cures more than 20 per cent of an appreciable proportion of the patients developing this disease. Judging by the Edinburgh experience, after megavoltage irradiation, although local failure is common, the expectation of long survival is better than it is after operation. The main reason for this difference is the absence of treatment mortality following irradiation.

For carcinoma of the lower thoracic esophagus, surgery is quite frequently successful and of proved value in a large series of patients. At this level radiotherapy has not yet received an adequate trial but should probably be preferred to surgery for patients over the age of 60 to 65 years and for patients who for other reasons are not good surgical risks.

In Edinburgh the value of megavoltage irradiation is being investigated when used as the only initial treatment for squamous cell carcinoma at all levels in the esophagus, including the cardia. Twenty out of 99 patients are alive 5 years after irradiation, each has a normal stomach, a normal voice, is well nourished and leads a normal life.

Department of Radiotherapy
University of Edinburgh
The Royal Infirmary
Edinburgh, 3
Scotland

I am deeply indebted to my colleagues in the radiotherapy and surgical departments in Edinburgh for asking me to treat their patients, for making numerous useful suggestions and for allowing me free access to their records, to Mrs. Jackie Badstevener for preparing the diagrams, to Mr. Ronnie Robertson for the photographs and to Mrs. Grace Butt for the typescript.

REFERENCES

1. Bergman, F. Cancer of oesophagus: histological study of development and local spread of 10 cases of squamous cell carcinoma in lower third of oesophagus. *Acta chir. scandinav.*, 1959, *117*, 356–365.
2. Buschke, F. Surgical and radiological results in treatment of esophageal carcinoma. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1954, *71*, 9–24.
3. Dunlop, E. E. Carcinoma of oesophagus with survival. *Australian & New Zealand J. Surg.*, 1960, *30*, 81–91.
4. Fleming, J. A. C. Carcinoma of thoracic oesophagus. *Brit. J. Radiol.*, 1943, *16*, 212–216.
5. Fleming, J. A. C. Radiotherapy in cancer of thoracic oesophagus. *Thorax*, 1947, *2*, 206–215.
6. Leborgne, R., Leborgne, F., Jr., and Barlocci, L. Cancer of esophagus: results of radiotherapy. *Brit. J. Radiol.*, 1963, *36*, 806–811.
7. le Roux, B. T. Analysis of 700 cases of carcinoma of hypopharynx, oesophagus, and proximal stomach. *Thorax*, 1961, *16*, 226–225.
8. le Roux, B. T. Influence of resection on natural history of carcinoma of hypopharynx, esophagus, and proximal stomach. *Surg., Gynec. & Obst.*, 1962, *115*, 162–170.
9. Logan, A. Surgical treatment of carcinoma of esophagus and cardia. *J. Thoracic & Cardiovasc. Surg.*, 1963, *46*, 150–161.
10. McCort, J. J. Radiographic identification of lymph node metastases from carcinoma of esophagus. *Radiology*, 1952, *59*, 694–711.
11. Marcial, V. A., Tomé, J. M., Ubiñas, J., Bosch, A., and Correa, J. N. Role of radiation therapy in esophageal cancer. *Radiology*, 1966, *87*, 231–239.
12. Miller, C. Carcinoma of thoracic oesophagus and cardia: review of 405 cases. *Brit. J. Surg.*, 1962, *49*, 507–522.
13. Morson, B. C. Spread of carcinoma of oesophagus. In: Neoplastic Disease at Various Sites. Volume IV. Tumours of the Oesophagus. Edited by Tanner and Smithers. E. &. S. Livingstone, Ltd., Edinburgh, 1961, pp. 136–145.
14. Mustard, R. A. Selection of therapy for esophageal cancer. *A.M.A. Arch. Surg.*, 1957, *75*, 674–679.
15. Nakayama, K. Pre-operative irradiation in treatment of patients with carcinoma of oesophagus and of some other sites. *Clin. Radiol.*, 1964, *15*, 232–241.
16. Nakayama, K., Orihata, H., and Yamaguchi, K. Surgical treatment combined with preoperative concentrated irradiation for esophageal cancer. *Cancer*, 1967, *20*, 778–788.
17. Pearson, J. G. Radiotherapy of carcinoma of oesophagus and post cricoid region in South East Scotland. *Clin. Radiol.*, 1966, *17*, 242–257.
18. Pierquin, B., Tubiana, M., and Dutreix, J. Étude de 54 cas de cancers de l'oesophage thoracique traités par le betatron 22 MeV. *J. de radiol., d'électrol. et de méd. nucléaire*, 1958, *39*, 725–736.
19. Pierquin, B., Wambersie, A., and Tubiana, M. Cancer of thoracic oesophagus: two series of patients treated by 22 MeV betatron. *Brit. J. Radiol.*, 1966, *39*, 189–192.
20. Scanlon, E. F., Morton, D. R., Walker, J. M., and Watson, W. L. Case against segmental resection for esophageal carcinoma. *Surg., Gynec. & Obst.*, 1955, *101*, 290–296.
21. Seaman, W. B., and Ackerman, L. V. Effect of radiation on esophagus: clinical and histologic study of effects produced by betatron. *Radiology*, 1957, *68*, 534–540.
22. Smithers, D. W. Radiotherapy of carcinoma of oesophagus. In: Neoplastic Disease at Various Sites. Volume IV. Tumours of the Oesophagus. Edited by Tanner and Smithers. E. & S. Livingstone, Ltd., Edinburgh, 1961.
23. Veraguth, P. In: Le Cancer de l'Oesophage. Edited by G. Candardjis. Masson et Cie, Paris, 1963.
24. Watson, T. A. Radiation treatment of cancer of esophagus. *Surg., Gynec. & Obst.*, 1963, *117*, 346–354.
25. Watson, W. L., Goodner, J. T., Miller, T. P., and Pack, G. T. Torek esophagectomy: case against segmental resection for esophageal cancer. *J. Thoracic Surg.*, 1956, *32*, 347–359.

SOME OPINIONS ON TREATMENT OF CANCER OF THE ESOPHAGUS*

By W. D. RIDER, M.B., *and* R. DIAZ MENDOZA, M.D.
TORONTO, ONTARIO, CANADA

THE experience with cancer of the esophagus at the Princess Margaret Hospital and its predecessor, The Ontario Institute of Radiotherapy, has been previously reported.[1] During the period under review, 1950 to 1964, some 446 cases have been seen. There has been no fixed policy of referral or management—each case has been treated on its own merits by individual radiotherapists, and frequently the influence of referral has had a bearing on the method of treatment employed. As a result of this type of policy, a variety of methods have been tried, with varying degrees of success. It is unfortunate that there are not enough cases from which to make statistical deductions in any one particular treatment group; on the other hand, there are several very strong "clinical impressions."

Since 1950, there has been a steady increase in the number of cases referred for radiotherapy and this is probably due to several factors. The availability of supervoltage equipment, the increase in number and age of population, and, perhaps, the impressive value of palliation have in some measure contributed to this increase (Fig. 1). Although the number of cases has increased, there has been little change in the median survival time, and this probably reflects the inclusion of more advanced cases which, in the past, would not have been offered any treatment. At any rate, there is one glimmer of hope, inasmuch as there were no 5 year survivors prior to 1954, whereas now there are some.

Analysis by technique, dose, or by any of the common parameters is fraught with difficulty due, as previously mentioned, to the small number of cases in each group. The various methods of treatment used

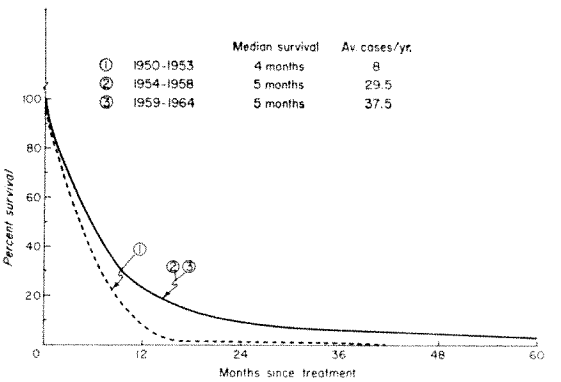


FIG. 1. Carcinoma of esophagus. Survival by "Quinquennia."

and the median and 3 year survival results are tabulated (Table 1).

If the patients treated with radical intent are considered, it is evident that with smaller volumes in particular, and lower doses in general, there is a slight improvement in the survival pattern. It has been possible to analyze dose only in a rather crude way. This reveals that there are no survivors at 5 years of patients who received less than 4,500 rads. There are between 10 and 20 per cent survivors in the range of 4,500 to 5,500 rads, and no survivors in the over 6,000 rad range where the total radiation was delivered by external beam in the conventional "5 fractions and about 1,000 rads per week" without correction for lung factor.

Perhaps it is worth commenting upon the evolution of some of the techniques used, if only in an historical sense. It has followed the classical clinical pattern of impressions gleaned from the previous 2 or 3 cases, and falls in line with the usual practice of medicine.

In the late forties and early fifties a feeling of pessimism existed in the manage-

* Presented at the Fiftieth Annual Meeting of the American Radium Society, Miami Beach, Florida, April 7–11, 1968.
From the Princess Margaret Hospital, Toronto, Ontario, Canada.

TABLE I

CANCER OF ESOPHAGUS 1950–1964

No. of Cases	Technique	Dose (rads)	Time (days)	Volume 100 ml. (per cent)	Median Survival (months)	3 Year Crude Survival (per cent)	Comments
21	No Treatment	—	—	—	4	0	
148	Palliative Irradiation	2-4,000	5–28	Various	5	0	
55	Irradiation and Surgery	← Various →			—	~ 8	
Upper Third							
5	Orthovoltage 200–400 kv.	6,000	35	250	6	0	
3	Co^{60} and Ra Bougie	7,000	28	<100	5	0	Necrosis in 3 cases
39	Co^{60} alone	6,500	42	<250	7	10	
Lower Two-Thirds							
14	Orthovoltage 200–400 kv.	4,500 5,000	28 35	600	7	0	
32	Co^{60} 360° Rotation	5,000 6,000	27 32	250 400	5	0	
51	Co^{60} 6 Oblique Fields (Manchester Style)	5,500 6,500	32 42	425	6	4	Pulmonary fibrosis
45	Co^{60} 4 Oblique Fields	5,500	35	400 700	10	9	
21	22 mev. Roentgen Rays 3 Fields	6,000 6,500	38 42	250	12	17	Pulmonary fibrosis
12	Co^{60} and Ra Bougie	7,000	24–38	100	24	37	
446							

ment of cancer of the esophagus. The temporary benefit which followed orthovoltage irradiation was often viewed as making the patient "die twice" but, on the other hand, the surgical mortality was so high that there was little choice.[3]

When "horendotrons"[4] become available in the form of cobalt 60 teletherapy units, linear accelerators, and betatrons, a new era was opened. The immediate results were striking from a symptomatic point of view; most patients were relieved of their dysphagia. Postmortem examinations in many of these early cases, however, showed that there was residual tumor in the treatment volume. It was, therefore, quite natural that the dose of radiation should be increased; in spite of this, no improvement in survival rates occurred, although the "rate of relief of dysphagia" did increase. It was some time before the pattern of late death due to cor pulmonale following radiation fibrosis of the lungs became manifest. This was due, in part, to the fact that many of the patients returned home, at long distances from Toronto, and were never seen again at the hospital. Death was usually ascribed to cancer and frequently not even a chest roentgenogram was made, or if one was, the appearance was reported as "lymphangitic spread" of cancer. In reviewing this material retrospectively, it is believed that the incidence of pulmonary fibrosis was somewhere between 5 and 50 per cent, depending upon technique, and that with the 6 field technique for tumors below the aortic arch, it approached 80 per cent. With tumors in the upper third of the esophagus, a smaller amount of pulmonary tissue is traversed by the radiation beam and the fibrosis produced is less liable to give rise to cardiac complications; the remaining lung is able to compensate.

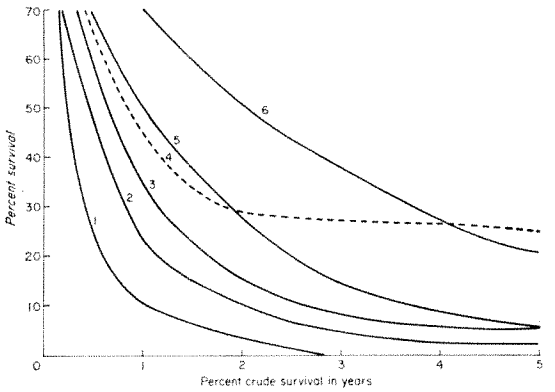


FIG. 2. Carcinoma of esophagus (1950–1964). Cases treated radically. Techniques: 1. Co^{60} rotation; 2. Co^{60} 6 oblique fields; 3. Co^{60} 4 oblique fields; 4. Pearson technique (Edinburgh), 4 mev. roentgen rays; 5. 22 mev. roentgen rays 3 fields; and 6. Co^{60}+radium bougie (see Table 1 for details).

The survival pattern obtained by our major techniques (Fig. 2) has been compared with data kindly supplied by Pearson,[8,9] being the best available radiation information at the present time. It is apparent that 2 of the Princess Margaret Hospital techniques give slightly better early results, but there is a more pronounced and continuing loss of patients with the progress of time. The exact cause of this difference is not clear, part of it may be due to late cardiac complications, but in a small number of autopsies and the occasional patient submitted to thoracotomy, at least part of it was due to recurrence of cancer. It is not possible to make a statistical analysis because of the low autopsy and operation rates.

Mention must be made of the small group of patients who were treated by a combined approach—that of external beam irradiation followed by the insertion of a radium loaded esophageal bougie. Obviously, this is a selected series, but probably no more selected than those treated by operation alone, or by preoperative irradiation. The usual method of treatment has been to give 3,500 to 4,000 rads external Co^{60} radiation in a period of $3\frac{1}{2}$ to 4 weeks to the whole mediastinum and follow this by the insertion of a radium bougie on 3 consecutive days. The dose delivered is 1,000 rads per day, as measured on the surface of the bougie which has a diameter of 13 mm. Thus a maximum tissue dose of 7,000 rads is achieved in a period of about 4 to 5 weeks. When the fate of these patients was reviewed in detail, it was found that if the radium bougie was inserted immediately after the external beam irradiation, necrosis occurred commonly; if, however, there was an interval of a week or more between these 2 procedures, necrosis was absent. One patient treated by this method has survived 11 years.

Can anything be learned from a study of this kind? The comment that cancer of the esophagus is a lethal disease needs no further emphasis, nor does the aspect of pulmonary fibrosis already mentioned. The problem of failure to control the primary tumor is a serious one, since this can occur in spite of high doses of radiation delivered to the right area.

Cancer of the esophagus tends to affect the older age group in which cardiovascular changes are often present. Jenkin and Stryker,[1] from this Institute, have shown a good correlation between hypertension and survival rate in cancer of the cervix—the hypertension appears not only to protect the tumor but also the normal tissue from the effects of radiation. While there is no proof, it is suggested that this is an oxygen effect and it would be most surprising if this effect did not occur in squamous cell cancers in other sites. Thus, it might account, to a degree, for some of the "radioresistance" in cancer of the esophagus. If there is any logic to this reasoning, then these patients should benefit from hyperbaric oxygen radiotherapy. At the same time much more investigation along cardiovascular lines might well be rewarding.

Many patients who die soon after irradiation, do so as the result of perforation of a contiguous viscus—the aorta, trachea or bronchus. This is due to the "formation" of a fistula by destruction of the intervening tumor. Some of these problems can be anticipated if the tumor is identified in

the trachea or bronchus at the time of endoscopy, but the spread of cancer into the aorta is, at the present time, not readily detected. Better methods of evaluation are required to determine the extent of the cancer before deciding upon either radiation therapy or surgery. As Watson[10] has pointed out, one of the more frustrating aspects of the disease is that of having to sail between "Scylla and Charybdis," of treating a large enough volume to include the tumor and its metastases and not too large to give rise to complications.

One of the disappointments in this study has been the failure to control more cases by rotation therapy. The rotation units are equipped with transmission dose measuring chambers[2] so that it should be possible to estimate the esophageal dose more accurately than with any of the "lung correction" methods. In spite of this, and on the whole, with somewhat lower doses, there has been no improvement in the results. This problem requires further study, both by the radiotherapist and the physicist.

The experience in the past 4 years is somewhat anecdotal because of the influence stimulated by other centers. Preoperative irradiation has been tried, along the lines advocated from Japan,[6] in a small number of cases—with unsatisfactory results. Postoperative irradiation equally has not made its mark. On the whole, tumor doses in the 5,000 rad in 4 week range are employed at the present time.[8,9]

In the period under review, 55 cases were treated by a combination of irradiation and surgery: 34 cases after surgical failure, with 2 survivors at 5 years; and 21 cases after irradiation followed by surgery, again with 2 survivors. These figures however, have little meaning because of the selection and since the 2 postirradiation survivors did not have tumor at operation.

It is quite obvious that the present state of management of cancer of the esophagus leaves much to be desired and that future progress must assuredly be along the lines of different radiobiologic concepts. The place of surgery is likely to be one of replacement, once the transplantation rejection problems have been mastered.

SUMMARY

1. The fate of 446 patients with cancer of the esophagus treated mainly with irradiation, between 1950 and 1964, is reviewed.

2. The results of all methods used are tabulated.

3. A comparison is made with the best radiation data available and this suggests that some of the deaths are related to radiation complications.

4. Some suggestions regarding investigation and treatment are made.

W. D. Rider, M.B.
Princess Margaret Hospital
500 Sherbourne Street
Toronto 5, Ontario
Canada

REFERENCES

1. Jenkin, R. D. T., and Stryker, J. A. Influence of blood pressure on survival in cancer of cervix. *Ann. Roy. Coll. Phys. & Surgeons, Canada*, 1968, *1*, No. 1, p. 59.
2. Johns, H. E. The Physics of Radiology. Second edition. Charles C Thomas, Publisher, Springfield, Ill., 1961, pp. 427–430.
3. Mendoza, R. D. Cancer of esophagus: fifteen year review. D.M.R. Thesis, University of Toronto. Presented before Canadian Association of Radiologists, Feb., 1967.
4. Mustard, R. A. Selection of therapy for oesophageal cancer. *A.M.A. Arch. Surg.*, 1967, *95*, 674–679.
5. Mustard, R. A., and Ibberson, O. Carcinoma of esophagus: review of 381 cases admitted to Toronto General Hospital 1937–1953 inclusive. *Ann. Surg.*, 1956, *144*, 927–940.
6. Nakayama, K. Pre-operative irradiation in treatment of patients with carcinoma of oesophagus and some other sites. *Clin. Radiol.*, 1964, *15*, 232–241.
7. Patterson, J. F. Personal communication.
8. Pearson, J. G. Personal communication, 1968.
9. Pearson, J. G. Radiotherapy of carcinoma of oesophagus and post cricoid region in South East Scotland. *Clin. Radiol.*, 1966, *17*, 242–257.
10. Watson, T. A. Radiotherapy in treatment of cancer of oesophagus. *Radiol. Clin. & Biol.*, 1967, *36*, 1–14.

DOSIMETRIC CONSIDERATIONS IN COBALT 60 ROTATIONAL THERAPY FOR ESOPHAGEAL LESIONS*

A COMPARISON OF TRANSIT AND INTRALUMINAL DOSE MEASUREMENT

By DAVID B. GOLDENBERG, M.D., U. V. GOPALA RAO, ScD., STEWART LOTT, M.D., *and* JOSEPH DIGEL, R.T.
BALTIMORE, MARYLAND

IN 1957, the total incidence of carcinoma of the esophagus in the United States was reported to be approximately 4,500 cases, representing an annual incidence rate of 2.7 per hundred thousand population.[1] Radiation therapy and surgery both play a major role in the management of this disease. The opinion expressed by various authors is that the greatest usefulness of surgery is in lower third lesions.[3,6] Upper third lesions should probably all be treated primarily by supervoltage or telecobalt therapy.[6] Middle third tumors measuring more than 5 cm. in length are in general not curable by resection or irradiation, while those less than 5 cm. have about the same survival rate when treated either by radical surgery or radical radiation therapy. Rotational therapy is particularly applicable to this area.

Control of the primary lesion by radical dose radiation therapy is not unusual. Watson and Brown[9] emphasized this point when they reported the microscopic findings at autopsy in 4 patients who had been subjected to vigorous mediastinal irradiation. None had persistence of the primary neoplasm. The minimum curative dose is generally not less than 5,000 rads delivered to the tumor in less than 6 weeks.[6] Other authors suggest a tumor dose of 6,500 to 7,000 rads in 6 to 8 weeks.[6] Not only are intercomparisons of treatment results made difficult by this relatively wide variability in reported dose response, but dosage considerations are further complicated by inconsistencies in reporting radiation transmission through pulmonary parenchyma. Failure to account for this factor may result in serious overdosage of the esophagus as well as other mediastinal and thoracic structures.[8] Jacobson and Knauer[4] evaluated lung correction factors for fixed field Co^{60} teletherapy utilizing a pressdwood phantom with cork lungs. The correction factor obtained for simulated mediastinal lesions treated through 3 portals was 1.20. Watson[8] using multiple fixed field telecobalt radiotherapy for carcinoma of the esophagus obtained 10 to 40 per cent correction factors for each field by transit dose determinations. Jacobson and Knauer also evaluated rotational Co^{60} radiotherapy for simulated mediastinal lesions, again using a pressdwood phantom with cork lungs. With a 360° rotational field and a source axis distance (S.A.D.) of 115 cm., they found a correction of 1.15 for large fields (10×15 cm.) and 1.20 for small fields (7×7 cm.).

The investigation described herein was undertaken to determine lung correction factors under actual treatment conditions for esophageal carcinoma treated by rotational Co^{60} teletherapy, comparing estimated doses suitably corrected by transit dose measurements for increased lung transmission with those obtained by direct measurement using intraluminal dosimeters in the same patient. We were also interested in assessing whether a standard correction factor could be applied to all patients, or

* Presented at the Fiftieth Annual Meeting of the American Radium Society, Miami Beach, Florida, April 7–11, 1968.
From the Department of Radiology, Division of Radiotherapy, The Johns Hopkins Medical Institutions, Baltimore, Maryland.
This work was supported in part by USPHS Grant #5-T-01-GM 01328, from the National Institute of General Medical Sciences.

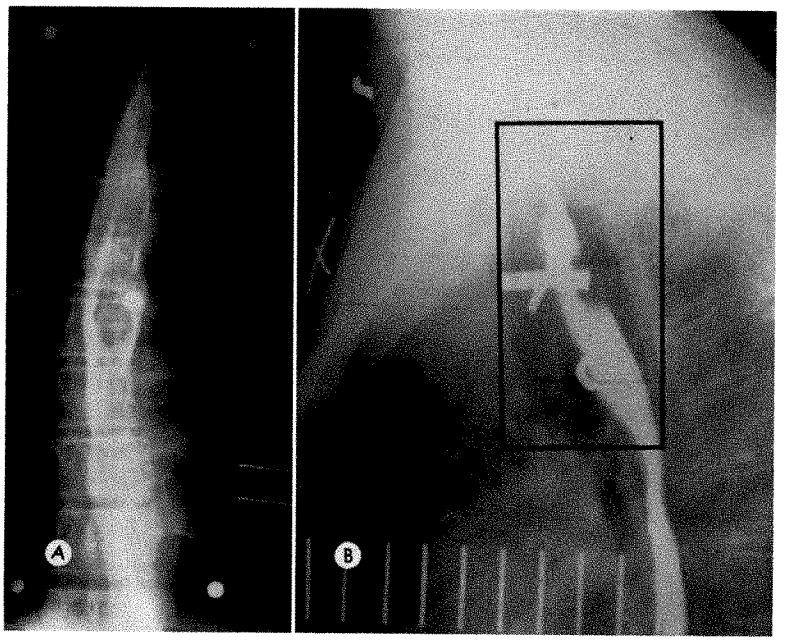


FIG. 1. Carcinoma of the middle third of the esophagus. (*A*) Anteroposterior and (*B*) lateral supine roentgenograms for localization of the esophagus showing the treatment volume and magnification markers.

whether individual patient variability would preclude the use of such a correction.

METHOD

Eight patients with proven squamous cell carcinoma of the middle third of the esophagus were treated with a cobalt 60 teletherapy unit (Atomic Energy of Canada Limited "Theratron 80") by 360° rotation therapy technique at a source tumor distance (S.T.D) of 80 cm. The tumor volume in each patient was localized on a transverse contour of the thorax by means of frontal and lateral roentgenograms with barium in the esophagus (Fig. 1, *A* and *B*). Employing an isocentric dose distribution (Fig. 2), radii from the center of the esophagus to the edge of the body contour were measured every 20 degrees to obtain an average radius. Using this measurement and the appropriate tissue-air ratio, the time required to deliver a prescribed dose at the tumor center was obtained, without taking into account any possible increase in tumor dose due to transmission of radiation through the lung.[5] Each patient was then treated for the time thus determined and a measurement of the transit dose was made using a Victoreen condenser r chamber mounted on the back shield of the therapy unit, with the center of the chamber aligned to the central axis of the radiation beam. After completion of the treatment, a measurement of dose at the same position was made under identical conditions (leaving the table in place) but without the patient in the beam. A ratio of these two measurements yielded the transit dose ratio from which the effective soft tissue thickness of the patient was determined by means of calibration curves previously obtained from measurements made on a tissue equivalent phantom. One-half of the body thickness thus obtained yielded the effective average radius. From a knowledge of the tissue air ratio for this radius, the actual dose delivered at the center of rotation was estimated.[5]

During another treatment on the same patient a direct intraluminal dose measurement was made using a Siemens' condenser chamber with an effective volume of 0.5 cc.

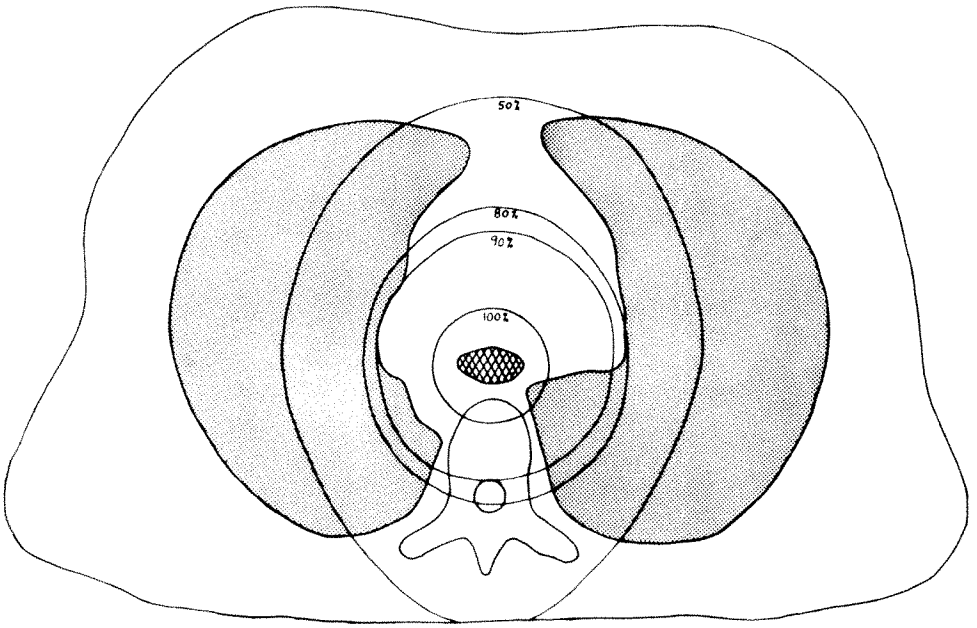


FIG. 2. Isodose distribution for 360° rotational cobalt 60 teletherapy of carcinoma of the middle third of the esophagus. A field size of 14 cm.×8 cm. and a source tumor distance of 80 cm. were used.

This chamber was previously calibrated with a standard Victoreen dosimeter, which in turn had been calibrated at the National Bureau of Standards. A metallic marker was then placed at the center of the treatment field and the esophageal dosimeter positioned. A check roentgenogram was obtained to ascertain that the tip of the dosimeter corresponded to the center of the treatment field (Fig. 3). The patient was then treated and the tumor dose measured.

RESULTS AND DISCUSSION

It was initially noted that a discrepancy existed between intraluminal and transit dose measurements, the intraluminal doses measuring consistently 8 per cent higher (range 1.04–1.11). Three possible reasons for this observed difference have been considered. The first is the possibility that the intraluminal dosimeter was incorrectly placed in the esophagus. This was immediately ruled out, since in all patients a metallic marker was placed at the center of the treatment field, the esophageal dosimeter positioned, and a check roentgenogram obtained to ascertain that the tip of the dosimeter corresponded to the center of the treatment field (Fig. 3).

A second possibility is, that since the esophagus lies just posterior to the center of the body, a false transit dose reading might be obtained. This was checked by making phantom measurements and found to be not true.

The third possibility, that of a temperature correction, was then considered. Since the intraluminal dosimeter was used at body temperature, it was thought that a correction factor for chamber air density should have been applied. This possibility was tested experimentally by exposing the dosimeter to the radiation beam at normal room temperature (72.0°F.) and at body temperature (98.6°F.). The approximate correction factor so obtained was 5 per cent. Thus, it was apparent that the major cause of the discrepancy between transit and intraluminal dose measurements could be accounted for by temperature dependence of the intraluminal dosimeter. The final results are presented in Table 1. It is apparent that there is agreement within 3 per cent between the average temperature corrected intraluminal dose and the average dose as measured by the transit method.

An additional finding is the wide range of the correction factors (6–27 per cent) ob-

served from patient to patient. In order to assess whether this might be accounted for by individual patient variation, an attempt was made in each case to evaluate the effect of the field size, tumor location, body weight, and apparent lung density as observed in chest roentgenograms. A ratio of the per cent of solid tissue to lung tissue was also made using lateral and frontal chest roentgenograms. While the means of measurement of these parameters may have been too inexact to allow a precise evaluation of their effect, no consistent correlation could be found between these factors and the magnitude of the correction. It was concluded that because of the observed wide range of correction values, a standard correction factor for increased lung transmission as advocated by Batho[2] and others could not be consistently applied and that actual dose measurements are therefore necessary in each case. Because of patient comfort and the possibility of perforating a diseased esophagus, transit dose measurements would appear to be the method of choice.

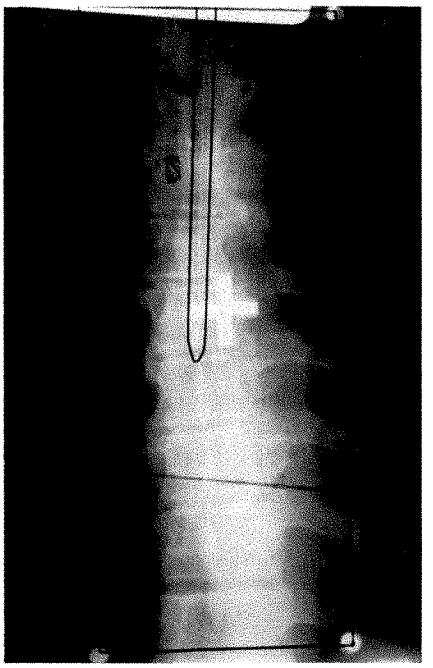


Fig. 3. Check localization roentgenogram showing the tip of the intraluminal dosimeter in the esophageal lumen in relation to skin marker locating center of esophageal treatment volume.

Table I

ESOPHAGEAL DOSE MEASUREMENTS

Field Size (cm.)	Calculated Single Dose (rads) at the Center of Rotation Neglecting Lung Transmission	Intraluminal Dose Measurement (rads)	Transit Dose Measurement (rads)	Intraluminal Dose Correction Factor	Intraluminal Correction Factor; Corrected for Temperature	Transit Dose Correction Factor
5×15	200	208	222	1.04	1.09	1.11
8×14	275	308	332	1.12	1.18	1.21
8×14	275	290	300	1.06	1.10	1.10
7×18	200	226	252	1.13	1.19	1.26
7×18	200	234	248	1.17	1.23	1.24
5×12	240	280	305	1.17	1.23	1.27
6×14	240	240	254	1.00	1.05	1.06
6×21	187	200	225	1.07	1.12	1.20
			Average	1.10	1.15	1.18

CONCLUSIONS AND SUMMARY

1. When esophageal dosage is measured with a temperature corrected intraluminal dosimeter and the measurements compared in the same patients with transit corrected dose measurements, agreement is obtained to within 3 per cent. Because of patient comfort and the possibility of perforating a diseased esophagus, the transit dose method appears to be the best and most practical means of obtaining such measurements.

2. The wide range of lung correction factors observed would seem to indicate that the application of one standard correction factor in all patients is not desirable. A transit corrected dose measurement should be made in each case.

David B. Goldenberg, M.D.
Department of Radiology
The Johns Hopkins Hospital
601 N. Broadway
Baltimore, Maryland 21205

The authors wish to thank Mrs. Marylee Turner for her assistance in the preparation of the manuscript.

REFERENCES

1. ACKERMAN, L. V., and DEL REGATO, J. A. Cancer: Diagnosis, Treatment and Prognosis. Third edition. C. V. Mosby Company, St. Louis, 1962.
2. BATHO, H. F. Lung corrections in cobalt 60 beam therapy. *J. Canad. A. Radiologists*, 1964, *15*, 79–83.
3. BUSCHKE, F., and CANTRIL, S. T. Results of supervoltage roentgenotherapy of esophageal carcinoma. *J. Thoracic Surg.*, 1953, *26*, 105–108.
4. JACOBSON, L. E., and KNAUER, I. S. Correction factors for tumor dose in chest cavity due to diminished absorption and scatter in lung tissue. *Radiology*, 1956, *67*, 863–876.
5. JOHNS, H. E. The Physics of Radiology. Second edition. Charles C Thomas, Publisher, Springfield, Ill., 1961.
6. MARCIAL, V. A., TOMÉ, J. M., UBIÑAS, J., BOSCH, A., and CORREA, J. N. Role of radiation therapy in esophageal cancer. *Radiology*, 1966, *87*, 231–239.
7. SMITH, I. H. Cobalt 60 Teletherapy; A Handbook for the Radiation Therapist and Physicist. Paul B. Hoeber, Inc., New York, 1964.
8. WATSON, T. A. Radiation treatment of cancer of esophagus. *Surg., Gynec. & Obst.*, 1963, *117*, 346–354.
9. WATSON, T. A., and BROWN, E. M. X-ray therapy in carcinoma of esophagus. *J. Thoracic Surg.*, 1951, *22*, 216–218.

Vol. 105, No. 3

SURGICAL AND RADIATION TREATMENT OF CANCER OF THE THORACIC ESOPHAGUS*

By JOHN T. GOODNER, M.D., F.A.C.S.†
NEW YORK, NEW YORK

A REPORT on the treatment of all cases of cancer of the thoracic esophagus seen at Memorial Hospital between 1926 and 1966, or for a period of over 40 years, is presented. Prior to 1940, all cases were treated with some form of radiation therapy.[5] The most important part of this report dates from 1940, when the first case of cancer of the esophagus was treated by surgical excision. The cases seen which were treated elsewhere, those that had no definitive treatment, and those that had treatment without histologic or cytologic proof of the disease have been eliminated. The predominance of these eliminated cases were those seen early in the series, that is, between 1926 and 1940.

MATERIAL

The total number of cases of cancer of the esophagus seen at Memorial Hospital between the years 1926 and 1966 inclusive was 1,859. There were 192 cases of primary cancer of the cervical esophagus, leaving a total of 1,667 cases of cancer of the thoracic esophagus. Of the cases in which cancer involved the thoracic esophagus the following have been eliminated: 171 cases without histologic or cytologic proof, 292 cases in which there was no definitive treatment and 93 cases treated elsewhere. Thus, there were 1,111 proved and treated cases of cancer of the thoracic esophagus. Of this total, 851 cases were treated by irradiation alone and 260 cases treated surgically, or 23.4 per cent in which the primary lesion of the esophagus was excised. These 260 cases make the basis of this report (Table 1).

TABLE I

MEMORIAL HOSPITAL
CANCER OF THE ESOPHAGUS
1926–1966

Total number of cases		1,859
Cervical esophageal cancer		192
Thoracic esophageal cancer		1,667
Cases without histologic proof	171	
Cases not treated	292	
Cases treated elsewhere	93	
Proven cases treated at Memorial Hospital (thoracic cancer)		1,111
Treated by radiation therapy alone		851
Treated surgically (resection)		260

SURGICAL PROCEDURES

The type of surgical procedure used was divided into 8 groups. Thoracic esophagectomy alone, without re-establishment of continuity, was the first type of procedure used at Memorial Hospital starting in 1940; there were 36 cases in this group.

In 1942, the first esophagectomy combined with esophagogastrostomy was performed. This was the largest group and there were 164 cases, 9 of whom are 5 year survivors. Three of the 9 had radiation therapy in addition to their surgery. Thus, the 5 year survival rate in this group of 164 cases is 5.4 per cent. There were an additional 3 cases in which the esophagogastrostomy was delayed, or the above operation was done in 2 stages. In 4 cases the stomach had to be excised in addition to the esophagus, leading to an esophagojejunostomy to restore continuity. There were 5 cases in which a staged procedure was carried out, and in which a jejunal transplant was used to restore continuity following the esophagectomy. There has been 1 long survivor in this group of 5, or 20 per cent. He is still alive 19 years after resection.

In 1955, the first colon transplant was performed. It was thought that in these debilitated, elderly patients, esophagec-

* Presented at the Fiftieth Annual Meeting of the American Radium Society, Miami Beach, Florida, April 7–11, 1968.
† Associate Attending Surgeon, Thoracic Service, Memorial Hospital, and Instructor in Surgery, Cornell University Medical School, New York, New York.

TABLE II

MEMORIAL HOSPITAL
CANCER OF THE ESOPHAGUS

Type of Surgery	No. of Cases	5 Year Survivors
Esophagectomy alone	36	
Esophagectomy and esophagogastrostomy	164	9 (3) (5.4%)
Esophagectomy and delayed esophagogastrostomy	3	
Esophagogastrectomy and esophagojejunostomy	4	
Esophagectomy and delayed jejunal transplant	5	1 (20%)
Esophagectomy and delayed colon transplant	31	6 (3) (19.3%)
Esophagectomy preceded by colon transplant	14	
Esophagectomy, miscellaneous	3	
Total	260	16 (6.1%)

tomy with esophagogastrostomy was too much surgery at one time, that a staged procedure was safer, and that the use of the colon instead of the stomach might physiologically be an improvement in the surgical treatment of this disease. Since 1955, there have been 31 cases in which esophagectomy was followed by colon transplant at a later date.[6] There are 6 in this group who have survived over 5 years, 3 having had additional radiation therapy. The survival rate is 19.3 per cent.

In 1956, a preoperative irradiation program was inaugurated in the hope of improving our results in the treatment of this disease.[1] However, it prolonged our treatment time, as a waiting period was necessary before surgical excision of the esophagus was deemed advisable. Prolongation of the treatment period was added to by the additional colon transplant which was eventually necessary to restore continuity.

In 1960, in order to decrease the length of the treatment period, it was decided to perform the colon transplant prior to esophagectomy, during the waiting period following radiation therapy. Since 1960, there have been 14 cases in which colon transplant preceded the esophagectomy. There were 3 miscellaneous cases, of little significance, but they complete the series (Table II).

TABLE III

MEMORIAL HOSPITAL
CANCER OF THE ESOPHAGUS
SEX INCIDENCE IN SURGICAL CASES

	Females	Males
Esophagectomy alone	4	32
Esophagectomy and esophagogastrostomy	42	122
Esophagectomy and delayed esophagogastrostomy	0	3
Esophagogastrostomy and esophagojejunostomy	1	3
Esophagectomy and delayed jejunal transplant	1	4
Esophagectomy and delayed colon transplant	11	20
Esophagectomy preceded by colon transplant	0	14
Miscellaneous	0	3
Total	59	201

SEX INCIDENCE

Of the 260 cases in which resection of the esophagus was carried out there were 201 males and 59 females (Table III).

PATHOLOGY

Most of the cases were squamous cell or epidermoid carcinomas. There were 238 of this type. In addition, there were 15 adenocarcinomas, 4 sarcomas, and 1 each of melanoma, mucoepidermoid and oat cell carcinoma.

ESOPHAGECTOMY ALONE

In this group of 36 cases, 1 case was lost to follow-up and there were 11 postoperative deaths. Thus there were 24 cases in

TABLE IV

MEMORIAL HOSPITAL
CANCER OF THE ESOPHAGUS
ESOPHAGECTOMY ALONE

Number of cases	36
Lost to follow-up	1
Postoperative deaths	11
Determinate cases	24
Average survival in months	9.7
Preoperative irradiation	8
Survival	8.3
Postoperative irradiation	2
Survival (6 and 18 mo.)	12.0

which survival could be determined. In this 24, the average survival was 9.7 months. Eight cases received preoperative irradiation and survived an average of 8.3 months after surgery (average of 12.5 months post-irradiation). Two patients received postoperative irradiation surviving 6 and 18 months, respectively (Table IV).

ESOPHAGECTOMY AND ESOPHAGOGASTROSTOMY

In this group of 164 cases, there were 3 lost to follow-up and 42 postoperative deaths. Four are still alive, thus leaving 115 determinate cases. Two of those still alive had surgery over 5 years ago, and there are an additional 7 who survived 5 or more years. The average survival in these 115 cases is 18 months if the 7 cases are included and 15 months if they are not included. In 25 cases postoperative irradiation was given immediately or at a later date. One of these survived only 6 days following surgery, the remaining 24 having an average survival of 9.9 months. However, two survived for 5 years. Preoperative irradiation was given in 14 with an average survival of 21 months, 1 having survived 5 years (Table V).

TABLE V

MEMORIAL HOSPITAL
CANCER OF THE ESOPHAGUS
ESOPHAGECTOMY AND ESOPHAGOGASTROSTOMY

Number of cases	164
Lost to follow-up	3
Postoperative deaths	42
Still alive	4
Determinate cases	115
Survivors of 5 or more years	7
Average survival in months (115)	
If 7 included	18.0
If 7 excluded	15.0
Postoperative irradiation	25
1 postoperative death—6 days	
24 with average survival	9.9
2 survived 5 years	
Preoperative irradiation	14
Average survival	21.0
1 survived 5 years	

TABLE VI

MEMORIAL HOSPITAL
CANCER OF THE ESOPHAGUS
ESOPHAGECTOMY AND DELAYED ESOPHAGO-GASTROSTOMY

Number of cases	3
Average postresection survival	6.3
Postoperative irradiation	1
Average postoperative survival	7.0
Average postirradiation survival	5.0
Preoperative irradiation	2
Average postoperative survival	6.0
Average postirradiation survival	9.0

ESOPHAGECTOMY AND DELAYED ESOPHAGOGASTROSTOMY

In the 3 cases in this group the average postresection survival was 6.3 months. One patient received postoperative irradiation surviving 7 months after operation and 5 months following irradiation. The remaining 2 had preoperative irradiation and survived an average of 6 months after operation and 9 months following irradiation (Table VI).

ESOPHAGOGASTRECTOMY AND ESOPHAGOJEJUNOSTOMY

Of the 4 patients in this group the average survival was 4 months. None of the patients received irradiation (Table VII).

TABLE VII

MEMORIAL HOSPITAL
CANCER OF THE ESOPHAGUS
ESOPHAGOGASTRECTOMY AND ESOPHAGOJEJUNOSTOMY

Number of cases	4
Number irradiated	0
Average survival in months	4.0

TABLE VIII

MEMORIAL HOSPITAL
CANCER OF THE ESOPHAGUS
ESOPHAGECTOMY AND DELAYED JEJUNAL TRANSPLANT

Number of cases	4
Average postresection survival (1 still alive after 19 years)	13.4
No irradiation	2
Postoperative irradiation	2
Average postoperative survival	15.0
Average postirradiation survival	14.0

ESOPHAGECTOMY AND DELAYED JEJUNAL TRANSPLANT

There were 5 cases in which a segment of jejunum was used to restore continuity of the alimentary canal. One of these is still alive after 19 years. The average postresection survival in the remaining 4 patients was 13.4 months. Two patients did not receive radiation therapy and 2 had postoperative irradiation. In the latter 2 cases, the average postresection survival was 15 months and the average postirradiation survival was 14 months (Table VIII).

ESOPHAGECTOMY AND DELAYED COLON TRANSPLANT

Of the 31 cases in this group, 5 are still alive, one surviving over 3 years and 4 surviving 5 or more years. There are thus 26 cases in which survival has been determined. The average postresection survival is 20.8 months. There are 4 patients in which death occurred in the postoperative period following the colon transplant with an average survival of 11 days. The average post-transplant survival in the remaining 22 patients was 22.2 months. Postoperative irradiation was given in 3 patients with an average postresection survival of 9.7 months and an average postirradiation survival of 1.6 months. Seventeen patients received preoperative irradiation. On the average, they survived 22.8 months following irradiation and 19.2 months after resection. In addition to the 4 patients that have survived more than 5 years and are still alive, there is 1 patient in this group that survived 11 years following his resection and died of another cause. Thus there are 2 that survived 5 years and 3 that survived 7, 11 and 12 years, respectively. The 2 that survived 7 and 12 years are still alive. They and the 1 that expired after 11 years received no irradiation (Table IX).

ESOPHAGECTOMY PRECEDED BY COLON TRANSPLANT

In the 14 cases in this group 1 was lost to follow-up and there were 3 deaths in the immediate postresection period with an average survival of 6 days. In the remaining 10 cases, the average postresection survival was 8.8 months. The average post-transplant survival was 10 months. Preoperative irradiation was given in these 10 cases with an average postirradiation survival of 12.0 months (Table X).

MISCELLANEOUS GROUP

There were 3 cases remaining in the 260 cases which received surgical treatment that did not fall into the other groups. One patient had restoration of esophageal continuity by means of a buried skin graft. He survived 8 months after resection and 5 months following esophagoplasty. The sec-

TABLE IX

MEMORIAL HOSPITAL
CANCER OF THE ESOPHAGUS
ESOPHAGECTOMY AND DELAYED
COLON TRANSPLANT

Number of cases	31
Still alive	5
Surviving 3 years—1	
Surviving 5 or more years—4	
Determinate cases	26
Average postresection survival	20.8
Postoperative deaths (post-transplant)	
Average survival—11 days	4
Average post-transplant survival (22)	22.2
Postoperative irradiation	3
Average postresection survival	9.7
Average postirradiation survival	1.6
Preoperative irradiation	17
Average postirradiation survival	22.8
Average postresection survival	19.2
Five year survivors	
2–5 years	
3–7, 11 and 12 years	

ond case had a total esophagectomy with pharyngogastrostomy surviving 48 months, but he required radiation therapy for recurrent disease 11 months prior to his demise. The third case had esophagectomy and colon transplant in one stage, surviving only 6 days. He had preoperative irradiation 3 months prior to his death.

PREOPERATIVE IRRADIATION

Since the inauguration of this program in 1956, there have been 85 cases treated in this manner through 1966. Those cases which had a previous or a coexistent primary cancer elsewhere in the body, those with distant metastases from the esophageal cancer, and those with a medical condition which precluded surgery were excluded from the program. Of the 85 cases treated with preoperative irradiation, 47 or 55.2 per cent were resected; 12 or 14.1 per cent were found to be nonresectable; and, 26 or 30.5 per cent never came to surgery. Of those that completed the program, there are 2 still alive and surviving over 5 years. One died after surviving almost 7 years, and 1 survived almost 4 years before being lost to follow-up. In the remaining 44, the average postirradiation survival was 14.1 months. There were 7 postoperative deaths. In the remaining 37 cases the average postoperative survival was 13.1 months.

OPERABILITY AND RESECTABILITY

At 5 year intervals, the operability and resectability rates have been determined. In 1944, when the number of cases operated upon was 41, the resectability rate was 34.2 per cent. At the end of our present report with 260 cases resected, the resectability rate stands at 61.0 per cent (Table XI).

Table X

MEMORIAL HOSPITAL
CANCER OF THE ESOPHAGUS
ESOPHAGECTOMY PRECEDED BY COLON TRANSPLANT

Number of cases	14
Lost to follow-up	1
Postoperative deaths (postresection)	3
Average survival	6 days
Determinate cases	10
Average postresection survival	8.8
Average post-transplant survival	10.0
Preoperative irradiation	10
Average postirradiation survival	12.0

CONCLUSIONS AND SUMMARY

In the presurgical era, it was found that the use of radiation therapy in the treatment of cancer of the esophagus could cause disappearance or decrease in the size of the tumor. However, there was usually a recurrence of the disease within a few months.

Because of the poor results with surgery alone, a preoperative irradiation program was instituted, and surgery was performed to remove the tumor before it had a chance to recur. In 7 cases there was no evidence of cancer in the resected specimen. We believe that preoperative irradiation will not affect the 5 year survival rate, but that it does increase the resectability rate.

Table XI

MEMORIAL HOSPITAL
RESECTABILITY IN CANCER OF THORACIC ESOPHAGUS

Year	No. of Cases	No. Explored	Not Resected	Resected	Operability (per cent)	Resectability (per cent)
1944	227	41	27	14	18.0	34.2
1949	482	133	71	62	27.5	46.6
1954	748	256	115	141	34.2	55.0
1959	980	348	149	199	35.5	57.1
1964	1,176	410	163	247	34.8	60.2
1966	1,241	426	166	260	34.3	61.0

Our 5 year survivors, from irradiation alone, from surgery alone or with the combined treatment appear to be sporadic cases that survive in small groups and the cause of their survival is not evident.

It does appear that better results can be obtained when smaller lesions are treated, and thus the key to improved treatment results lies in an earlier diagnosis.

653 Park Avenue
New York, New York 10021

REFERENCES

1. CLIFFTON, E. E., GOODNER, J. T., and BRONSTEIN, E. Preoperative irradiation for cancer of esophagus. *Cancer*, 1960, *13*, 37–45.
2. CLIFFTON, E. E., and GOODNER, J. T. Integrated treatment of carcinoma of esophagus. In: Cancer Therapy by Integrated Radiation and Operation. Edited by B. F. Rush, Jr., and R. H. Greenlaw. Charles C Thomas, Publisher, Springfield, Ill., 1968, pp. 60–66.
3. WATSON, W. L., and GOODNER, J. T. Carcinoma of esophagus. *Am. J. Surg.*, 1957, *93*, 259–265.
4. WATSON, W. L., and GOODNER, J. T. Carcinoma of esophagus. *J. Internat. Coll. Surgeons*, 1957, *28*, 715–723.
5. WATSON, W. L., and GOODNER, J. T. Radiation treatment of esophageal cancer. In: Treatment of Cancer and Allied Diseases. Volume IV. Edited by G. T. Pack, and I. M. Ariel. Hoeber Medical Division, Harper & Row, Publisher, New York, 1960, pp. 591–599.
6. WATSON, W. L., and CLIFFTON, E. E. Total esophagoplasty using right colon. *Cancer*, 1957, *10*, 488–496.

VOL. 105, NO. 3

RADIATION INDUCED NEOPLASIA FOLLOWING EXTERNAL BEAM THERAPY FOR CHILDREN WITH RETINOBLASTOMA*

By ROBERT H. SAGERMAN, M.D.,† J. ROBERT CASSADY, M.D.,† PATRICIA TRETTER, M.D.,† *and* ROBERT M. ELLSWORTH, M.D.‡
NEW YORK, NEW YORK

THE occurrence of benign and malignant neoplasms following radiation therapy has been previously documented in the radiologic literature.[1,3–5,12,18,19,22] Reese *et al.*,[14] Forrest,[7] and, more recently, Soloway[20] have recorded instances of neoplasia following irradiation for retinoblastoma. The purpose of this report is to detail the experience with radiation induced neoplasms in children treated for retinoblastoma in the Retinoblastoma Clinic of the Institute of Ophthalmology and the Radiotherapy Division of the Columbia-Presbyterian Medical Center; 21 cases are presented, 11 for the first time, including the previously unreported development of thyroid carcinoma in 2 patients treated with radium brachytherapy. The incidence of radiation induced neoplasia is correlated with dose, the latent period until the clinical appearance of the radiation induced neoplasm determined and correlated with dose, and the decreased risk of this complication with current treatment methods, are emphasized.

MATERIAL

Six hundred and twenty-five patients were registered in the Retinoblastoma Clinic from 1930 through 1963; 92 were seen before 1945, 186 from 1946 through 1954, and 347 thereafter. Of these, 397 received radiation therapy; the remainder were treated surgically, either for unilateral disease or when disease was so advanced that no hope of retaining vision remained. In 243 of these 397, follow-up data are available for 5 or more years; of the remainder, 81 died of retinoblastoma, 5 died of intercurrent disease, and 68 were lost to follow-up or are not eligible for 5 year analysis.

METHOD

During these 34 years, three general treatment policies have been followed. From 1930 to 1945, the technique described by Reese and his associates[14] was used. With this method, orthovoltage radiation was given to an ipsilateral direct lateral field and to a contralateral oblique nasal field using a 3 cm. diameter cone. An exposure dose of 7,000–9,000 r was given to each field, for a combined exposure dose of 14,000–18,000 r (approximately 11,000–14,000 r tumor dose). Beginning in 1945, most patients were treated with the same technique but with a reduction in the combined exposure dose to 7,5000–8,000 r (approximately 6,000–6,500 r tumor dose). The third policy began in the early 1950s with the use of a single direct lateral field and the delivery of a tumor dose of 3,500–4,500 r; this was initially accomplished with kilovoltage equipment until a megavoltage unit became available in 1957. Several patients received a second course of radiation therapy following initial treatment failure, with occasional tumor control and long-term survival.

Treatments have been given on a three times a week basis throughout. Field size has varied from a 3 cm. diameter circle to a 4 cm.×5 cm. rectangle. With kilovoltage radiation the dose in compact bone is approximately 2.1 times, and the dose in the "soft tissue" component of bone approximately 1.6 times, the soft tissue tumor

* Presented at the Fiftieth Annual Meeting of the American Radium Society, Miami Beach, Florida, April 7–11, 1968.
From the Department of Radiology, Division of Radiotherapy,† and the Institute of Ophthalmology, Retinoblastoma Clinic,‡ of the Columbia-Presbyterian Medical Center, New York, New York.

TABLE I

HISTOLOGIC DIAGNOSIS

Histopathology	No.
Osteosarcoma	9
Fibrosarcoma	2
Sarcoma, unspecified	2
Thyroid, papillary-follicular	2
Squamous cell carcinoma	2
Histiocytoma, malignant fibrous	1
Mesenchymoma, malignant	1
Rhabdomyosarcoma	1
Basal cell carcinoma	1
	21

dose.[8] Currently, 3,500 rads is reached in 18–20 days using 22.5 mev. photons through a 3 cm.×4 cm. lateral field.

RESULTS

A second malignant tumor appeared in 23 patients. Two cases of osteosarcoma developed in the femur, outside the treatment field, and are not thought to represent radiation induced tumors, leaving 21 cases for analysis. A histologic diagnosis was established in each patient (Table I).

There were 10 males and 11 females; the sex ratio in retinoblastoma is 1:1. The age at diagnosis of retinoblastoma in these patients ranged from 6 weeks to 6 years with a mean of 2 years (Table II). The latent period from conclusion of radiation therapy to the initial signs and/or symptoms of the second neoplasm ranged from 4 to 30 years, with a mean of 11 years. The greatest number of cases appeared in the fifth post-treatment year (Fig. 1). There was no apparent correlation between dose and latent period.

Table III shows the incidence of neoplasia development correlated with dose for those children followed for a minimum of 5 years. Although the numbers are small, the incidence seems to fit a quadratic rather than a linear relationship.

The summary of modified life table analysis of all patients receiving radiation therapy is presented in Table IV. The three time periods analyzed correspond to the three general treatment policies noted above. There has been a significant reduction in the risk of developing a radiation tumor with the lower doses now in use.

Development of radiation neoplasm carries a grave prognosis. Only 6 of these 21 patients are now alive. Three of these 6 have required several operations plus radiation therapy to control disease; one boy is clinically stable 8 months after irradiation for a nonresectable sarcoma involving the brain. Table V summarizes the pertinent information for each patient.

As previously noted, 2 girls in this series were treated by means of radium tubes on a tray which was placed lateral to the eye for a predetermined period of time. Both patients subsequently developed histologically proven adenocarcinoma of the thyroid.

REPORT OF CASES

CASE 1. Bilateral retinoblastoma was diagnosed and the left eye enucleated on December 16, 1930 in a 4 year old girl. Exenteration of the left orbit was deemed necessary as the optic nerve was infiltrated with tumor on histologic examination. Radiation therapy was undertaken for the right eye. Four radium applications (1/wk.) were made in January, 1931 to a total of 6,000 mg. hr. The radium was filtered with 3 mm. brass and was situated approximately 3 cm. lateral to the patient's right eye. The approximate exposure dose at the eye and thyroid was 3,600 r and 400 r, respectively. No other history of radiation exposure *in utero* or childhood could be discovered.

The patient was well until age 14 years (May, 1941) when left cervical lymphadenopathy was noted. This progressed and in October, 1941, a left thyroidectomy and left radical neck dissection were performed. Histopathologic ex-

TABLE II

AGE AND SEX DISTRIBUTION OF 21 PATIENTS WITH RADIATION INDUCED NEOPLASIA

Age (yr.)	<1	1	2	3	4	5	6	Total
Male	6	2				1	1	10
Female	3	1	1	5	1			11
Total	9	3	1	5	1	1	1	21

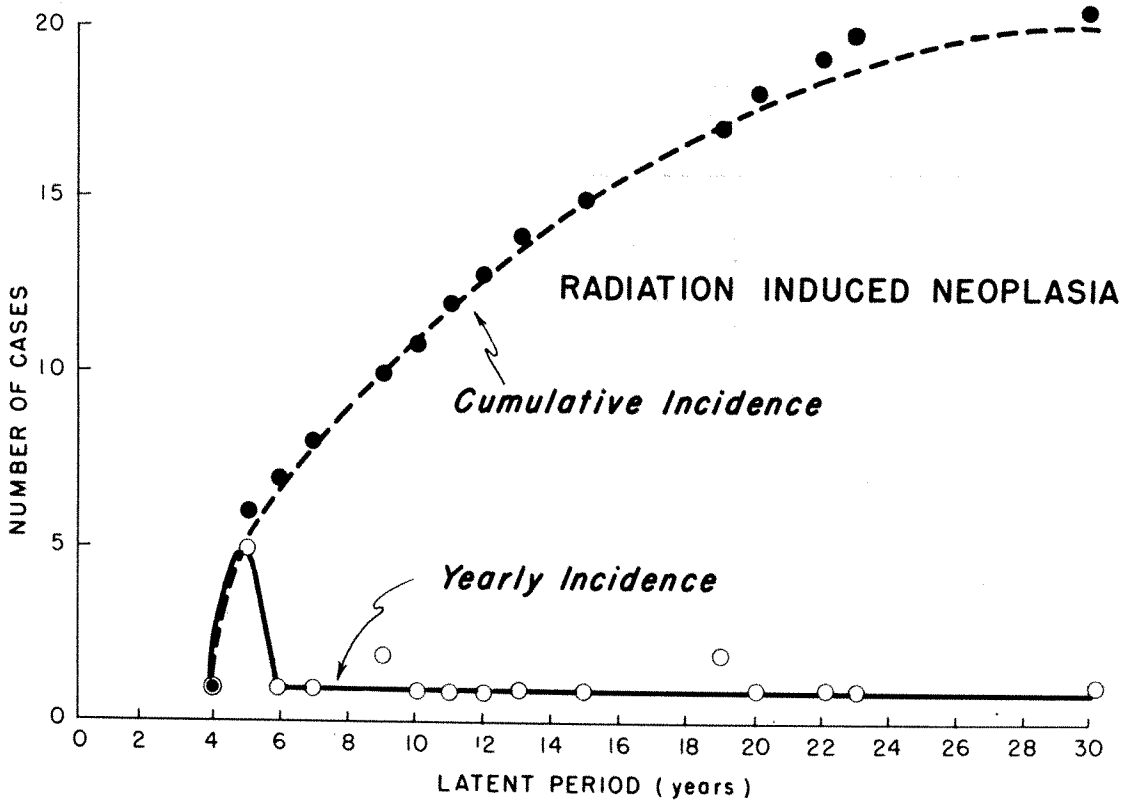


FIG. 1. Yearly and cumulative incidence of radiation induced neoplasia. Note the apparent threshold at 4–5 years and the relatively large incidence during the fifth post-treatment year.

amination showed a multifocal papillary adenocarcinoma of the thyroid gland with several lymph node metastases. In June, 1943, radical neck dissection was required for right cervical lymphadenopathy. Recurrent cervical and supraclavicular lymph nodes developed and lung metastases appeared. Death, secondary to disseminated metastatic thyroid carcinoma, occurred at age 27 years (February, 1954), 13 years after diagnosis of this neoplasm.

CASE 7. Enucleation of the left eye for retinoblastoma was performed in this 7 week old girl

TABLE III

INCIDENCE OF RADIATION INDUCED NEOPLASIA CORRELATED WITH DOSE

Tumor Dose (r)*	No. of External Beam Radiation Induced Tumors†	No. at Risk‡	Per Cent
<6,000	3	121	2.5
6,000–10,999	4	73	5.5
11,000–15,000	12	38	32.
Total	19	232	

* No correction applied for increased absorption in bone with kilovoltage radiation.

† Excludes 2 cases of thyroid carcinoma.

‡ 243 patients followed for 5 or more years minus 9 patients for whom no dose data were available minus 2 with thyroid carcinoma.

TABLE IV

SUMMARY OF MODIFIED LIFE TABLE ANALYSIS OF ALL PATIENTS RECEIVING RADIATION THERAPY

Period	Risk of Developing a Radiation Tumor	Standard Error
1930–1945	0.379	0.0347
1946–1954	0.206	0.0916
1955–1963	0.015	0.0106

1930–45 *vs.* 1946–54, Z = 1.76
1930–45 *vs.* 1955–63, Z = 9.05*
1946–54 *vs.* 1955–63, Z = 1.87

The three comparisons were evaluated at an over-all 5 per cent level of significance.

* Significant difference (Z = 2.41).

TABLE V

SUMMARY OF ALL PERTINENT INFORMATION IN THE PATIENTS STUDIED

Case No.	Year of Treatment	Age at Treatment	Estimated Tumor Dose†	Latent Period	Histopathology of Radiation Induced Tumor	Previously Reported*	Result
1	1931	4 yr.	Case report	10 yr.	Thyroid-papillary adenocarcinoma	No	Died of neoplasm
2	1933	6 yr.	19,000 r	7 yr.	Rhabdomyosarcoma	Yes[14]	Died of neoplasm
3	1935	3 yr.	19,000 r	30 yr.	Skin—squamous cell carcinoma	No	Alive (surgery +irradiation)
4	1936	5 yr.	2,400 r	9 yr.	Skin—basal cell carcinoma	Yes[14]	Alive (excision)
5	1937	3 yr.	15,000 r	13 yr.	Sarcoma—unspecified type	No	Died of neoplasm
6	1938	2 mo.	11,000 r	22 yr.	Osteosarcoma	Yes[20]	Died of neoplasm
7	1940	2 yr.	Case report	19 yr.	Thyroid—papillary and follicular adenocarcinoma	No	Alive (total thyroidectomy)
8	1942	6 mo.	12,000 r	9 yr.	Fibrosarcoma	Yes[7]	Died of neoplasm
9	1943	1 yr.	12,500 r	11 yr.	Lacrimal sac—squamous cell carcinoma	Yes[7]	Died of neoplasm
10	1943	6 mo.	12,500 r	15 yr.	Malignant mesenchymoma	Yes[7]	Died of neoplasm
11	1944	10 mo.	12,500 r	20 yr.	Osteosarcoma	Yes[20]	Died of neoplasm
12	1944	10 mo.	12,500 r	23 yr.	Osteosarcoma	No	Alive (surgery +irradiation)
13	1945	6 mo.	12,500 r	5 yr.	Osteosarcoma	No	Died of neoplasm
14	1947	3 yr.	12,500 r	4 yr.	Osteosarcoma	Yes[7]	Died of neoplasm
15	1948	7 mo.	10,500 r	19 yr.	Osteosarcoma	No	Died of neoplasm
16	1950	6 wk.	12,000 r	12 yr.	Osteosarcoma	Yes[20]	Died of cerebral abscess
17	1950	1 yr.	9,000 r	5 yr.	Fibrosarcoma	Yes[7]	Died of neoplasm
18	1958	3 yr.	8,500 r	5 yr.	Osteosarcoma	No	Alive (surgery +irradiation)
19	1960	1 yr.	4,000 r	5 yr.	Malignant fibrous histiocytoma	No	Died of neoplasm
20	1960	4 mo.	3,500 r	6 yr.	Sarcoma—unspecified type	No	Alive (irradiation)
21	1961	3 yr.	8,000 r	5 yr.	Osteosarcoma	No	Died of neoplasm

* Reference number.

† Cases 19–21: megavoltage irradiation; remainder kilovoltage.

in September, 1940. Postoperative radium therapy was given in a fashion similar to the previous case, one treatment per week for 5 weeks, to the right eye. Unfortunately, the records of these treatments have been lost and, therefore, total dose and factors are not known; we have estimated the dose to the thyroid gland at 700 r, for 6,000 mg. hr., taking into account the physical size difference in these 2 patients. In August, 1942, recurrent retinoblastoma was discovered in the right eye. Radiation therapy was instituted via 2 fields (right temporal and left nasal). Treatments were given three times a week in 400 r exposure dose increments, to a total exposure dose of 8,000 r to each field. The technical factors were 250 kvp., 1.5 mm. Cu half-value layer. A posterior lens radiation cataract rapidly developed which caused poor vision. In 1954, plastic surgery was performed for bone hypoplasia secondary to irradiation.

A right thyroid mass was noted in October, 1959. Total thyroidectomy was performed and histopathologic examination revealed Grade 1 papillary and follicular carcinoma of the thyroid gland with one paraglandular lymph node metastasis. The patient is now alive (1967) without evidence of thyroid cancer or retinoblastoma, with 20/200 vision.

DISCUSSION

There exists an extensive literature documenting the occurrence and risk of radiation carcinogenesis and leukemogenesis with exposure at various ages (*in utero*,[10,21] infancy and childhood,[9,13] and in adults[4,12]), and with ionizing radiation from external as well as internal sources.[17] Such exposure has occurred incidentally or accidentally (*in utero*,[10,21] atomic bomb survivors[2,11]) or during the treatment of benign[6,9,16] or malignant[4,12] disease, and has been either total body (*in utero*,[10,21] atomic bomb survivors [2,11]) or limited to a region of the body.[4,12]

It has been difficult to establish a dose *vs.* radiation-tumor incidence for external

beam radiation therapy for many reasons. Radiation therapy is usually undertaken for patients with malignant tumors, of whom only a fraction can be cured. Of those cured, many will die of some other illness common to older people in a few years. Thus, there are relatively few disease survivors who live long enough to develop a radiation induced tumor, and who have been followed closely. Furthermore, variations in technique in the treatment of any one disease occur with time, and it requires a relatively large population at risk to find the few neoplasms induced by any one technique.

We are fortunate to have (1) a rather homogeneous population, (2) of young age, (3) with a single disease—retinoblastoma, (4) treated to a small and constant volume, (5) with a uniform technique differing, in essence, only in the absorbed dose, and (6) with a high survival rate.

The postirradiation tumors herein reported all developed in previously normal tissues, and without other obvious inciting agent. Sarcomas account for 75 per cent of the cases, and almost 50 per cent of the group are osteosarcomas (Table v). The prevalence of osteosarcoma is explained by the increased absorption in bone with kilovoltage radiation utilized prior to 1957. The lowest tumor dose giving rise to osteosarcoma was 8,000 r. Other neoplasms developed with lower doses, the lowest inciting dose being 3,500 r for external beam therapy.

The induction of thyroid carcinoma in retinoblastoma survivors has not been reported, but its appearance after doses to the thyroid gland estimated at 400 r and 700 r is not surprising considering previous experience with low dose exposure of this gland.[13] The technique used in these two instances has been abandoned, and additional cases are not expected to develop with the well collimated, small fields now in use. Malignant fibrous histiocytoma is another type of neoplasm not previously reported after irradiation.

There has been a gradual decrease in the tumor dose used to control retinoblastoma from approximately 14,000 r prior to 1945 to the current technique of 3,500–4,500 rads, with some transition years and with some patients receiving more than one course of irradiation. In addition, the risk of damage to irradiated bone has decreased by a factor of approximately 2 with the introduction of megavoltage equipment, and the incidence of all tumors and of osteosarcoma alone is significantly lower. It is not possible to determine what the true incidence of radiation induced neoplasia will be with the current radiotherapy schedule, since new cases are expected to develop with the passage of time; the minimum risk is approximately 1.5 per cent (Table iv).

Other large series[4,12] reported an incidence of radiation induced neoplasia of approximately 0.1 per cent. In contrast, our figures range from 2.5 per cent to 32 per cent, depending upon dose, when using the same type of analysis—the population at risk is that surviving 5 or more years. Several factors help to explain this discrepancy in incidence: (1) approximately 70 per cent of all children treated at the Retinoblastoma Clinic will be cured of retinoblastoma and will, therefore, be at risk for many years;[15] (2) the inducing doses of radiation in our patients were generally greater than the average curative dose of radiation probably used in the majority of patients in other series; (3) perhaps of more importance: the patients in our series were all children and all were under the age of 4 years when treated. It has frequently been postulated that radiation effects on young, more actively growing tissues are proportionately more pronounced and it is, therefore, tempting to suggest this as the principal explanation for the marked incidence difference observed. The appearance of 2 cases of osteosarcoma of the femur, one in a patient not irradiated, raises the possibility of an increased susceptibility to neoplasia in retinoblastoma patients; this is under investigation.

The clinical appearance and management of most of the radiation induced tumors occurred outside our institution. Valuable help in establishing the nature of the tumor reappearing in or about the treated eye is provided by the time interval since radiation therapy. Our data show a minimum latent period of 4+ years and a high incidence of radiation induced neoplasia appearing during the fifth post-treatment year. The overwhelming majority of retinoblastoma recurrences have become manifest before the fifth post-treatment year.

Surgical management is most often undertaken for radiation induced neoplasms. In two clinical situations, however, operation cannot cure the lesion: (1) when the tumor is not resectable; and (2) when postoperative recurrence appears. Thus, radiation therapy has been given in 4 of the 6 survivors (Table v). Complete clinical regression for 18 months (Case 3), and for 8 months (Case 20) has occurred following irradiation with curative intent in the 2 patients under our direct control.

SUMMARY

Radiation induced neoplasia was assessed in a uniform population—children treated with irradiation for retinoblastoma.

The incidence of radiation induced neoplasia varied with dose, and is estimated to be approximately 1.5 per cent with current techniques (megavoltage, 3,500 rads in 18–20 days, treatment three times a week).

There was no direct correlation of dose with latent period.

Robert H. Sagerman, M.D.
Division of Radiotherapy
Upstate Medical Center
750 East Adams Street
Syracuse, New York 13210

We thank the Msdms. M. Von Ahn and L. C. Jones, for invaluable assistance in gathering these data, Mrs. L. Turgeon for statistical aid, and the members of the Retinoblastoma Clinic of the Institute of Ophthalmology for permission to report these cases.

REFERENCES

1. BERDON, W. E., BAKER, D. H., and BOYER, J. Unusual benign and malignant sequelae to childhood radiation therapy: including "unilateral hyperlucent lung." AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1965, *93*, 545–556.
2. Biological Effects of Atomic Radiation: Summary Reports. National Academy of Sciences, National Research Council, Washington, D. C., 1956.
3. CAHAN, W. G., WOODARD, H. Q., HIGINBOTHAM, N. L., STEWART, F. W., and COLEY, B. L. Sarcoma arising in irradiated bone: report of eleven cases. *Cancer*, 1948, *1*, 3–29.
4. CASTRO, L., CHOI, S. H., and SHEEHAN, F. R. Radiation induced bone sarcomas: report of five cases. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1967, *100*, 924–930.
5. COHEN, J., and D'ANGIO, G. J. Unusual bone tumors after roentgen therapy of children: two case reports. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1961, *86*, 502–512.
6. COURT-BROWN, W. M., and DOLL, R. Leukemia and aplastic anemia in patients irradiated for ankylosing spondylitis. Med. Res. Council Spec. Rep. No. 295, 1957.
7. FORREST, A. W. Tumors following radiation about eye. *J. Am. Acad. Ophth. & Otolaryng.*, 1961, *65*, 694–717.
8. GOODWIN, P. N. Spectral measurements of 200 to 300 kV x-rays. *Radiology*, 1966, *87*, 205–213.
9. HANFORD, J. M., QUIMBY, E. H., and FRANTZ, V. K. Cancer arising many years after radiation therapy. *J.A.M.A.*, 1962, *181*, 404–410.
10. MACMAHON, B. Prenatal x-ray exposure and childhood cancer. *J. Nat. Cancer Inst.*, 1962, *28*, 1173–1191.
11. MOLONEY, W. C., and KASTENBAUM, M. A. Leukemogenic effects of ionizing radiation on atomic bomb survivors in Hiroshima City. *Science*, 1955, *121*, 308–309.
12. PHILLIPS, T. L., and SHELINE, G. E. Bone sarcomas following radiation therapy. *Radiology*, 1963, *81*, 992–996.
13. PIFER, J. W., TOYOOKA, E. T., MURRAY, R. W., AMES, W. R., and HEMPELMANN, L. H. Neoplasms in children treated with x-rays for thymic enlargement. I. Neoplasms and mortality. *J. Nat. Cancer Inst.*, 1963, *31*, 1333–1356.
14. REESE, A. B., MERRIAM, G. R., JR., and MARTIN, H. E. Treatment of bilateral retinoblastoma by irradiation and surgery. *Am. J. Ophth.*, 1949, *32*, 175–190.
15. REESE, A. B., and ELLSWORTH, R. M. Management of retinoblastoma. *Ann. New York Acad. Sc.*, 1964, *114*, 958–962.
16. RUBIN, P., RYPLANSKY, A., and DUTTON, A.

Incidence of pelvic malignancies following irradiation for benign gynecologic conditions. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1961, *85*, 503–514.

17. SEIDLIN, S. M., SIEGEL, E., YALOW, A. A., and MELAMED, S. Acute myeloid leukemia following prolonged iodine-131 therapy for metastatic thyroid carcinoma. *Science*, 1956, *123*, 800–801.
18. SKOLNIK, E. M., FORNATTO, E. J., and HEYDEMANN, J. Osteogenic sarcoma of skull following irradiation. *Ann. Otol., Rhin. & Laryng.*, 1956, *65*, 915–936.
19. SOLHEIM, O. P. Bone sarcomas following external irradiation. *Acta radiol.* (Therapy), 1967, *6*, 197–201.
20. SOLOWAY, H. B. Radiation-induced neoplasms following curative therapy for retinoblastoma. *Cancer*, 1966, *19*, 1984–1988.
21. STEWART, A., WEBB, J., GILES, D., and HEWITT, D. Malignant disease in childhood and diagnostic irradiation in utero: preliminary communication. *Lancet*, 1956, *2*, 447.
22. TEBBET, R. D., and VICKERY, R. D. Osteogenic sarcoma following irradiation for retinoblastoma. *Am. J. Ophth.*, 1952, *35*, 811–818.

THE INFLUENCE OF THE RELATIONSHIP "LOCAL TUMOR EXTENT-TIME" UPON THE EVOLUTION OF TUMORS OF THE NASOPHARYNX*

By J. F. BOHORQUEZ, M.D., D.M.R.T., F.F.R.†
LONDON, ENGLAND

THE treatment of carcinoma of the nasopharynx presents many problems to the radiotherapist and is rather disappointing. The results are poor in spite of the fact that it is a disease that may be slow in evolution and which may remain localized to the head and neck, or even to the nasopharynx itself, for months or years. In many of these cases the recurrence of the primary growth is apparently small and retreatment to the primary areas has been given with good results. Reports in the literature suggest that an increase in survival time has been achieved with these intensive and repeated treatments.

MATERIAL AND METHOD

The special anatomic relationship of the nasopharynx accounts for much in the clinical behavior of these tumors. As in most of the head and neck tumors, these anatomic relationships seem to dominate and determine the natural history of these tumors and the resulting clinical pictures. A proper understanding of their mode of spread in time and in space, and the influence of this spread upon lymph node involvement, treatment and survival time is essential to the correct interpretation of the clinical biologic potential of these tumors.

Ideally, the best way to study the evolution of any tumor would be to study a patient, who from the inception of his tumor could be followed at regular intervals to his death, thus following the disease through its different local pathways, preferable areas of invasion, regional lymph node involvement and distant metastasis without treatment being given. As this is not possible on moral, humanitarian, and scientific grounds, and in an effort to uncover as many facts as possible concerning the evolution of nasopharyngeal carcinomas, it was decided to study 152 cases of squamous cell and undifferentiated carcinomas of the nasopharynx seen at the Head and Neck Unit of the Royal Marsden Hospital between 1933–1960.

The total number of patients was divided into 5 groups according to the delay between the first presenting symptom and the beginning of treatment. These patients had a delay of 3, 6, 9, 12, and more than 12 months. The possible areas of spread were divided as follows: superior to the base of the skull; posterior to the prevertebral region; inferior to the oropharynx; anterior to the nasal cavity; orbital, divided into extracranial and intracranial type of spread; and laterally to the parapharyngeal space, divided into prestyloid and retrostyloid. The prestyloid compartment was further subdivided into anterior to the pterygoid muscles; inferior to the submaxillary fossa; and posterolateral to the parotid gland.

The tumors were staged according to the International Classification of the International Union against Cancer, T, N, M and all of them were proved cancer of the nasopharynx objectively and histologically. The correlation of these groups and areas of involvement with age, sex, histology, site of the lesion, initial symptoms, stage, lymph node involvement and survival time was then undertaken. The total survival time for tumors of the nasopharynx for this group of patients has already been published by Lederman[9,10] and is not the

* Presented at the Forty-ninth Annual Meeting of the American Radium Society, Toronto, Ontario, Canada, May 29–31, 1967.
From the Royal Marsden Hospital, London, England.
† At present: Associate Director, Radiation Therapy Department, Michael Reese Hospital and Medical Center, Chicago, Illinois.

TABLE I

DISTRIBUTION OF CASES ACCORDING TO SEX AND HISTOLOGY

	No.	Per Cent		No.	Per Cent
Total male	103	67.8	Total female	49	32.2
Total squamous cell carcinoma	44	28.9	Total undifferentiated carcinoma	108	71.1
Male/squamous cell carcinoma	29	19.1	Female/squamous cell carcinoma	15	9.9
Male/undifferentiated carcinoma	74	48.7	Female/undifferentiated carcinoma	34	22.4

object of this study, the main purpose of which is concerned with the clinical evolution and its influence upon lymph node involvement, treatment and survival time. Therefore, the history of all 152 patients was carefully studied and evaluated with the main aim to ascribe as precisely as possible the site of origin of the tumor, stage and the spread to the already mentioned areas. Symptoms, clinical features and roentgenographic findings were all used to determined the classification of the patient.

GENERAL CONSIDERATIONS

SEX AND HISTOLOGIC DISTRIBUTION

This is shown in Table I, where it is seen that the total male to female ratio is 2.1:1, which is in accordance with most reported series. This ratio remains about the same when the histology is either squamous cell or undifferentiated carcinoma.

AGE GROUP DISTRIBUTION

This is shown in Table II, where it is seen that the peak incidence is in the fifth and sixth decades (53.2 per cent). This also holds true for both male and female in either squamous cell or undifferentiated carcinoma, although the incidence rate of undifferentiated carcinomas is higher in the younger age groups and especially in the fourth decade. In the first and second decades all the tumors were undifferentiated.

DISTRIBUTION ACCORDING TO INITIAL SITE

This can be seen in Table III, the highest incidence being in the posterosuperior wall and the lowest in the anteroinferior wall. This pattern was found in both male and female and in both squamous cell and undifferentiated carcinomas.

DISTRIBUTION ACCORDING TO PRESENTING SYMPTOMS

These are shown in Table IV, where it is seen that nasal and auricular symptoms had the highest incidence. This pattern is noted in both male and female and in either squamous cell or undifferentiated carcinoma. Fifteen per cent presented with lymph node involvement as the initial symptom.

DISTRIBUTION ACCORDING TO DELAY

This is shown in Table V, where it is seen that the highest incidence falls in the groups with 0 to 6 months delay. This incidence is also true when it is correlated to both squamous cell and undifferentiated carcinoma and in the male population indicating, perhaps, that the majority of tumors are highly malignant. In the female population, however, the peak incidence is in the 3 to 9 months delay group and may indicate that women seek medical advice later than men, or that their tumors are slower in growth.

DISTRIBUTION ACCORDING TO STAGE

This is seen in Table VI, where the peak incidence is in T_3 tumors. This is true for both male and female with either squamous cell or undifferentiated carcinomas (65.7 per cent were in Stages T_3 and T_4).

DISTRIBUTION ACCORDING TO LYMPH NODE INVOLVEMENT

This is depicted in Table VII, where it is shown that the highest incidence rate is for

TABLE II

DISTRIBUTION OF CASES ACCORDING TO AGE GROUP

Years	10	20	30	40	50	60	70	80
Male/squamous-cell carcinoma	—	—	3	—	11	11	4	—
Male/undifferentiated carcinoma	3	7	7	14	21	15	6	1
Female/squamous cell carcinoma	—	—	—	3	4	4	4	—
Female/undifferentiated carcinoma	1	4	4	6	8	7	4	—
Total	4	11	14	23	44	37	18	1
Percentage	2.6	7.2	9.2	15.1	28.9	24.3	11.8	0.7
Male	3	7	10	14	32	26	10	1
Per cent of total	2.9	6.8	9.7	13.6	31.1	25.2	9.7	1.0
Female	1	4	4	9	12	11	8	—
Per cent of total	2.0	8.2	8.2	18.4	24.5	22.4	19.4	0.0
Squamous cell carcinoma	—	—	3	3	15	15	8	—
Per cent of total	0.0	0.0	6.8	6.8	34.1	34.1	18.2	0.0
Undifferentiated carcinoma	4	11	11	20	29	22	10	—
Per cent of total	3.7	10.2	10.2	18.5	26.9	20.4	9.3	0.0

fixed or bilateral lymph node involvement. If we break down these figures this is true for males, but the incidence of fixed or bilateral lymph node involvement drops from 42.7 per cent in the male to 34.7 per cent in the female. If we relate the lymph

TABLE III

DISTRIBUTION OF CASES ACCORDING TO INITIAL SITE

	RW	LW	PSW	AIW
Male/squamous cell carcinoma	6	6	15	2
Male/undifferentiated carcinoma	23	20	28	3
Female/squamous cell carcinoma	4	3	7	1
Female/undifferentiated carcinoma	8	12	13	1
Total	41	41	63	7
Percentage	27.0	27.0	41.4	4.6
Male	29	26	43	5
Per cent of total	28.2	25.2	41.7	4.9
Female	12	15	20	2
Per cent of total	24.5	30.6	40.8	4.1
Squamous cell carcinoma	10	9	22	3
Per cent of total	22.7	20.5	50.0	6.8
Undifferentiated carcinoma	31	32	41	4
Per cent of total	28.7	29.6	38.0	3.7

RW—Right Wall. LW—Left Wall. PSW—Posterosuperior Wall. AIW—Anteroinferior Wall.

TABLE IV

DISTRIBUTION OF CASES ACCORDING TO INITIAL SYMPTOM

	1	2	3	5	6	7
Male/squamous cell carcinoma	14	6	2	3	2	2
Male/undifferentiated carcinoma	27	19	12	8	2	6
Female/squamous cell carcinoma	4	5	2	1	1	2
Female/undifferentiated carcinoma	13	12	7	2	—	—
Total	58	42	23	14	5	10
Percentage	38.2	27.6	15.1	9.2	3.2	6.6
Male	41	25	14	11	4	8
Per cent of total	39.8	24.3	13.6	10.7	38.8	7.8
Female	17	17	9	3	1	2
Per cent of total	34.7	34.7	18.4	6.1	2.0	4.1
Squamous cell carcinoma	18	11	4	4	3	4
Per cent of total	40.9	25.0	9.1	9.1	6.8	9.1
Undifferentiated carcinoma	40	31	19	10	2	6
Per cent of total	37.0	28.7	17.6	9.3	1.9	5.6

1—Nasal; 2—auricular; 3—lymph node involvement; 5—pain; 6—central nervous system involvement; 7—any other symptom.

node involvement to the histology it will be found that undifferentiated tumors have a higher incidence of fixed or bilateral lymph nodes than squamous cell carcinoma, dropping from 42.6 per cent in the former to 34.1 per cent in the latter. It is

TABLE V

DISTRIBUTION OF CASES ACCORDING TO DELAY IN MONTHS

	0–3	3–6	6–9	9–12	12+
Male/squamous cell carcinoma	8	11	4	5	1
Male/undifferentiated carcinoma	23	18	9	10	14
Female/squamous cell carcinoma	5	2	3	1	4
Female/undifferentiated carcinoma	3	11	9	6	5
Total	39	42	25	22	24
Percentage	25.7	27.6	16.4	14.5	15.8
Male	31	29	13	15	15
Percent of total	30.1	28.1	12.6	14.6	14.6
Female	8	13	12	7	9
Per cent of total	16.3	26.5	24.5	14.3	18.4
Squamous cell carcinoma	13	13	7	6	5
Per cent of total	29.5	29.5	15.9	13.6	11.4
Undifferentiated carcinoma	26	29	18	16	19
Per cent of total	24.1	26.9	16.7	14.8	17.6

TABLE VI

DISTRIBUTION OF CASES ACCORDING TO STAGE

	T_1	T_2	T_3	T_4
Male/squamous cell carcinoma	5	5	12	7
Male/undifferentiated carcinoma	9	20	28	17
Female/squamous cell carcinoma	—	1	9	5
Female/undifferentiated carcinoma	3	9	14	8
Total	17	35	63	37
Percentage	11.2	23.0	41.4	24.3
Male	14	25	40	24
Per cent of total	13.6	24.3	38.8	23.3
Female	3	10	23	13
Per cent of total	6.1	20.4	46.9	26.5
Squamous cell carcinoma	5	6	21	12
Per cent of total	11.4	13.6	47.7	27.3
Undifferentiated carcinoma	12	29	42	25
Per cent of total	11.1	26.9	38.9	23.1

also found that the highest incidence of no lymph node involvement is found in the squamous cell type of tumor (40.9 per cent). On the whole, 71.6 per cent of our cases presented lymph node involvement.

DISTRIBUTION ACCORDING TO METASTASIS

This is shown in Table VIII, the total being 3.3 per cent with the higher incidence in the male population and in the undifferentiated carcinoma.

DISTRIBUTION ACCORDING TO INVADED AREAS

This is shown in Table IX, where it is seen that there is no invasion of the prevertebral space, of the orbit, by the intracranial route, or of the inferior and posterolateral prestyloid pharyngeal compartments. It is also evident, that the oropharynx and nasal cavity are followed by spread superiorly to the base of the skull, and that the anterior prestyloid parapharyngeal and the parapharyngeal retrostyloid compartments are the most frequently involved areas. There were also 20 cases (13 per cent) with roentgenologic evidence of destruction of the base of the skull without any other sign of superior involvement. If we accept Lederman's theory of the spread leap-frogging around the peritubal fascia, this will bring the total superior involvement to 29.4 per cent. The higher frequency of invasion of these areas is found in both male and female in either squamous cell or undifferentiated carcinoma, with a greater tendency of the squamous cell carcinoma to invade the base of the skull. The nasal cavity and the oropharynx are invaded almost twice as often as the base of the skull, and this is highly significant.

DISTRIBUTION ACCORDING TO INITIAL SITE CORRELATED WITH INVASION AREAS

This is seen in Table X. We divided both squamous cell and undifferentiated carcinomas into 5 groups according to delay of diagnosis in months (3, 6, 9, 12, and more than 12 months) from the time of the presenting symptoms to the time of diagnosis. In each group the initial site was correlated with the invasion area in order to see if it is possible to unveil any particular pattern of spread in each of these categories in relation

TABLE VII

DISTRIBUTION OF CASES ACCORDING TO LYMPH NODE INVOLVEMENT

	N_0	N_1	N_2	N_3
Male/squamous cell carcinoma	11	3	5	10
Male/undifferentiated carcinoma	16	3	21	34
Female/squamous cell carcinoma	7	2	1	5
Female/undifferentiated carcinoma	9	3	10	12
Total	43	11	37	61
Percentage	28.3	7.2	24.3	40.1
Male	27	6	26	44
Per cent of total	26.2	5.8	26.2	42.7
Female	16	5	11	17
Per cent of total	32.7	10.2	22.4	34.7
Squamous cell carcinoma	18	5	6	15
Per cent of total	40.9	11.4	13.6	34.1
Undifferentiated carcinoma	25	6	31	46
Per cent of total	23.1	5.6	28.7	42.6

to the possible route of spread. None was found, but if we disregard the time-delay and we correlate the initial site with the most commonly invaded areas as shown in Table x, we find that tumors of the posterosuperior wall spread superiorly to the base of the skull twice as often as tumors from the right or left lateral wall and that tumors of the anteroinferior wall do not spread to the base of the skull at all. It was also found that tumors of all the walls spread equally to the oropharynx and that tumors of both lateral walls and posterosuperior walls spread equally anteriorly to the nose and to the parapharyngeal prestyloid anterior compartment. In both squamous cell and undifferentiated carcinomas the delay time was correlated to both initial symptom and initial site and none was found.

TABLE VIII

DISTRIBUTION OF CASES ACCORDING TO METASTATIC INVOLVEMENT

	M_0	M_1
Male/squamous cell carcinoma	29	—
Male/undifferentiated carcinoma	69	5
Female/squamous cell carcinoma	15	—
Female/undifferentiated carcinoma	34	—
Total	147	5
Percentage	96.7	3.3
Male	98	5
Per cent of total	95.1	4.9
Female	49	—
Per cent of total	100.0	0.0
Squamous cell carcinoma	44	—
Per cent of total	100.0	0.0
Undifferentiated carcinoma	103	5
Per cent of total	95.4	4.6

DISTRIBUTION ACCORDING TO DELAY CORRELATED WITH STAGE

This is seen in Table xi. This writer calls clinical age of a tumor the relationship between time-delay and local extent of a tumor. Although he is fully aware that it is impossible in the light of our present knowledge to determine accurately the moment of inception of a tumor or the

TABLE IX

DISTRIBUTION OF CASES ACCORDING TO INVASION AREAS

	1	3	4	5	6B	7A	7D	8	9	No Area
Male/squamous cell carcinoma	7	6	7	—	—	4	2	1	1	10
Male/undifferentiated carcinoma	9	25	14	1	3	5	5	—	1	31
Female/squamous cell carcinoma	5	6	5	—	—	3	—	—	—	1
Female/undifferentiated carcinoma	4	6	10	—	1	5	2	—	—	14
Total	25	43	36	1	4	17	9	1	2	55
Percentage	16.4	28.3	23.7	0.7	2.6	11.2	5.9	0.7	1.3	36.2
Male	16	31	21	1	—	9	7	1	2	41
Per cent of total	15.5	30.1	20.4	1.0	8.7	0.0	6.8	1.0	1.9	39.8
Female	9	12	15	—	4	8	2	—	—	15
Per cent of total	18.4	24.5	30.6	0.0	8.2	16.3	4.1	0.0	0.0	30.6
Squamous cell carcinoma	12	12	12	—	—	7	2	1	1	11
Per cent of total	27.3	27.3	27.3	0.0	0.0	15.9	4.5	2.3	2.3	25.0
Undifferentiated carcinoma	13	31	24	1	4	10	7	—	1	45
Per cent of total	12.0	28.7	22.2	0.9	3.7	9.3	6.5	0.0	0.9	41.7

1—Superior spread to base of skull; 3—inferior spread to oropharynx; 4—anterior spread to nose; 5—posterolateral spread; 6B—orbital and extracranial spread; 7A—parapharyngeal, prestyloid and anterior spread; 7D—parapharyngeal and retrostyloid spread; 8—hypophyseosphenoidal spread; 9—retrosphenoidal spread.

reliability of a patient when relating his symptoms, to the clinician this clinical age could be relevant as to prognosis. It is seen in Table XI that Stage T_1 tumors are more preponderant in the Groups 0 to 6 months, perhaps reflecting more rapidly growing tumors and therefore causing earlier symptoms. Tumors of Stage T_2 and T_3 are more or less evenly distributed in all the groups, perhaps indicating an average tumor growth pattern. Tumors of Stage T_4 show a slight tendency toward a greater time-delay, possibly reflecting a very slow tumor growth pattern.

DISTRIBUTION ACCORDING TO ENERGY AND TUMOR DOSE

This is shown in Table XII. It can be seen that 74 per cent of cases were treated with 220 kv., 1.5 mm. Cu half-value layer and that in only 14 or 9 per cent of these cases was it possible to deliver a tumor dose considered cancerocidal for these tumors. This is obviously due to the energy employed regardless of the ingenuity in planning the treatment. It is also seen that in only 26 per cent of the cases was supervoltage used, and in only 22 or 14 per cent was a radical course given, mainly because in most of these cases the aim of the treatment could only be palliative due to the extent of the disease, or because the general condition of the patients was such as to preclude a radical course of treatment.

TABLE X

DISTRIBUTION OF CASES ACCORDING TO INITIAL SITE CORRELATED WITH INVASION AREAS

Initial site	1	3	4	7A	7D
Right lateral wall	6	11	9	4	2
Left lateral wall	4	15	14	8	3
Posterosuperior wall	15	11	12	5	4
Anteroinferior wall	—	6	1	—	—

1—Superior spread to base of skull; 3—inferior spread to oropharynx; 4—anterior spread to nose; 7A—parapharyngeal, prestyloid and anterior spread; 7D—parapharyngeal and retrostyloid spread.

TABLE XI

DISTRIBUTION OF CASES ACCORDING TO DELAY IN MONTHS CORRELATED WITH STAGING

	0–3	3–6	6–9	9–12	12+
Stage T_1 total	6	8	—	3	—
Squamous cell carcinoma	1	3	—	1	—
Undifferentiated carcinoma	5	5	—	2	—
Stage T_2 total	6	11	7	8	3
Squamous cell carcinoma	1	2	—	2	1
Undifferentiated carcinoma	5	9	7	6	2
Stage T_3 total	23	11	12	6	11
Squamous cell carcinoma	10	3	6	2	—
Undifferentiated carcinoma	13	8	6	4	11
Stage T_4 total	4	12	6	5	10
Squamous cell carcinoma	1	5	1	1	4
Undifferentiated carcinoma	3	7	5	4	6

TABLE XII

DISTRIBUTION OF CASES ACCORDING TO ENERGY AND TUMOR DOSE (IN RADS)

Energy	2–3,000	3–4,000	4–5,000	5–6,000	6–7,000	Total
HVT	7	15	38	39	14	113 = 74%
SVT	1	0	2	14	22	39 = 26%

HVT—High voltage therapy = 220 kv., 1.5 mm. Cu half-value layer. SVT—Supervoltage therapy = either Co^{60} teletherapy or 2 mev. roentgen therapy.

DISTRIBUTION ACCORDING TO 5 YEAR CRUDE SURVIVAL TIME

This is shown in Table XIII, where it is seen that the 5 year survival for the total population was 15.1 per cent. This remains about the same for both male and female patients, but undifferentiated carcinomas show a higher survival rate than squamous cell carcinomas, almost three times as much.

DISTRIBUTION OF 5 YEAR CRUDE SURVIVAL ACCORDING TO AGE GROUP

This is shown in Table XIV. It is seen that the peak 5 year survival rate for the total population is in the fourth decade, being 43 per cent. When we break down these figures, we realize that the highest survival remains in this group for both male and female, with 36 per cent for male and 55 per cent for female. If the histology is related to survival in age groups, the

TABLE XIII

SURVIVAL OF PATIENTS IN YEARS

	1	3	5
Male/squamous cell carcinoma	10	3	—
Male/undifferentiated carcinoma	18	11	15
Female/squamous cell carcinoma	2	1	3
Female/undifferentiated carcinoma	16	3	5
Total	46	18	23
Percentage	30.3	11.8	15.1
Male	28	14	15
Per cent of total	27.2	13.6	14.6
Female	18	4	8
Per cent of total	36.7	8.2	16.3
Squamous cell carcinoma	12	4	3
Per cent of total	27.3	9.1	6.8
Undifferentiated carcinoma	34	14	20
Per cent of total	31.5	13.0	18.5

TABLE XIV

5 YEAR SURVIVAL ACCORDING TO AGE GROUP DISTRIBUTION

Years	10	20	30	40	50	60	70
Total	4	11	14	23	44	37	18
5 Year survival	0	0	3	10	7	8	3
Percentage	0	0	21	43	16	22	17
Male	3	7	10	14	32	26	10
5 Year survival	0	0	3	5	5	4	2
Percentage	0	0	33	36	16	15	20
Female	1	4	4	9	12	11	8
5 Year survival	0	0	0	5	2	4	1
Percentage	0	0	0	55	17	36	12
Squamous cell carcinoma	—	—	3	3	15	15	8
5 Year survival	—	—	—	1	2	2	2
Percentage	0	0	0	33	13	13	25
Undifferentiated carcinoma	4	11	11	20	29	22	10
5 Year survival	0	0	3	9	5	6	1
Percentage	0	0	27	45	17	27	10

5 Year survival is actual number of patients living, not percentage.

fourth decade also contains the highest 5 year survival for squamous cell carcinoma with 33 per cent and for undifferentiated carcinoma with 45 per cent. There was no survival in the first or second decades.

DISTRIBUTION OF 5 YEAR CRUDE SURVIVAL ACCORDING TO INITIAL SITE

This is shown in Table XV, where it is seen that the lowest survival time is for tumors of the posterosuperior wall, which is about 14 per cent as opposed to about 30 per cent for the other walls. This lower survival rate is also maintained for both male and female patients and either squamous cell or undifferentiated carcinomas.

DISTRIBUTION OF 5 YEAR CRUDE SURVIVAL ACCORDING TO INITIAL SYMPTOM

This is shown in Table XVI. It is seen, interestingly enough, that the highest survival rate was in the group with lymph node involvement as presenting symptom, being about 35 per cent, perhaps reflecting more cases of undifferentiated carcinomas, which are possibly more susceptible to cure by radiotherapy. This seems to be the case, as is shown further in Table XX. No patient presenting with symptoms of central r vous system involvement lived 5 years : those presenting with pain also had a v

TABLE XV

5 YEAR SURVIVAL ACCORDING TO INITIAL SITI

	RW	LW	PSW	A
Total	41	41	63	
5 Year survival	10	12	8	
Percentage	24	29	13	
Male	29	26	43	
5 Year survival	5	8	6	
Percentage	17	31	14	
Female	12	15	20	
5 Year survival	5	4	2	
Percentage	42	27	10	
Squamous cell carcinoma	10	9	22	
5 Year survival	2	0	3	
Percentage	20	0	14	
Undifferentiated carcinoma	31	32	41	
5 Year survival	8	12	5	
Percentage	26	38	12	

RW—Right Wall. LW—Left Wall. PSW—Posterosu Wall. AIW—Anteroinferior Wall.

5 Year survival is actual number of patients livin percentage.

TABLE XVI

5 YEAR SURVIVAL ACCORDING TO INITIAL SYMPTOM

	1	2	3	5	6	7
Total	58	42	23	14	5	10
5 Year survival	13	8	8	1	0	2
Percentage	22	19	35	7	0	20
Male	41	25	14	11	4	8
5 Year survival	9	5	5	1	0	0
Percentage	22	20	36	9	0	0
Female	17	17	9	3	1	2
5 Year survival	4	3	3	0	0	2
Percentage	23	18	33	0	0	100
Squamous cell carcinoma	18	11	4	4	3	4
5 Year survival	1	2	1	1	0	2
Percentage	6	18	25	25	0	50
Undifferentiated carcinoma	40	31	19	10	2	6
5 Year survival	12	6	7	0	0	0
Percentage	30	19	37	0	0	0

1—Nasal; 2—auricular; 3—lymph node involvement; 5—pain; 6—central nervous system involvement; 7—any other symptom. 5 Year survival is actual number of patients living, not percentage.

low survival rate of about 7 per cent, the pain usually indicating malignant osteomyelitis, or cranial nerve involvement.

DISTRIBUTION OF 5 YEAR CRUDE SURVIVAL ACCORDING TO DELAY

This is shown in Table XVII, which is a very interesting table to analyze. It is seen that the total lowest survival rate is in the 0 to 3 month delay group, the peak total survival rate being in the 6 to 9 month delay group, and remaining rather stable for the 9 to 12 month and more than 12 month delay groups. This may be due to the fact that the former are more malignant tumors, therefore presenting earlier symptoms, while the latter are less malignant, slower growing tumors, and thus more susceptible to cure.

DISTRIBUTION OF 5 YEAR CRUDE SURVIVAL ACCORDING TO STAGE AND LYMPH NODE INVOLVEMENT

This is shown in Table XVIII, where it is seen that the highest total survival rate is in T_1, being 35 per cent, remaining high at 29 per cent for T_2 and dropping to 5 per cent for T_4. It is impossible to say whether male or female patients or squamous cell or undifferentiated carcinomas fare better. Based on lymph node involvement the highest survival rate is in N_0 with 30 per cent, and there is a slight drop in N_1 to 27 per cent, indicating that there is not too much difference in survival rate. It drops further to 15 per cent in N_3. From these cases it is also impossible to say whether male or female patients fare better. This table furthermore shows that T_1 and T_2 tumors respond equally well and the same applies for tumors N_0 and N_1.

DISTRIBUTION OF 5 YEAR CRUDE SURVIVAL ACCORDING TO INVASION AREAS

This is shown in Table XIX, where it is seen that the highest survival rate was in patients showing spread of the carcinoma to the oropharynx, the nose, and retrostyloid parapharyngeal areas, being around 22 per cent. No patient with tumors spreading to the anterior prestyloid parapharyngeal compartments survived and only 8 per cent of those with carcinoma spreading superiorly to the base of the skull lived 5 years.

TABLE XVII

5 YEAR SURVIVAL ACCORDING TO DELAY IN MONTHS

	0–3	3–6	6–9	9–12	12+
Total	39	42	25	22	24
5 Year survival	4	8	8	6	6
Percentage	10	19	32	27	25
Male	31	29	13	15	15
5 Year survival	2	5	5	5	3
Percentage	6	17	38	33	20
Female	8	13	12	7	9
5 Year survival	2	3	3	1	3
Percentage	25	23	25	14	30
Squamous cell carcinoma	13	13	7	6	5
5 Year survival	2	0	2	2	1
Percentage	15	0	28	33	20
Undifferentiated carcinoma	26	29	18	16	19
5 Year survival	2	8	6	4	5
Percentage	8	27	33	25	21

5 Year survival is actual number of patients living, not percentage.

TABLE XVIII

5 YEAR SURVIVAL ACCORDING TO STAGE AND LYMPH NODE INVOLVEMENT

	Stage				Lymph Node Involvement			
	T_1	T_2	T_3	T_4	N_0	N_1	N_2	N_3
Total	17	35	63	37	43	11	37	61
5 Year survival	6	10	14	2	13	3	7	9
Percentage	35	29	22	5	30	27	19	15
Male	14	25	40	24	27	6	26	44
5 Year survival	4	7	7	2	7	1	6	6
Percentage	29	28	17	8	26	17	23	14
Female	3	10	23	13	16	5	11	17
5 Year survival	2	3	7	0	6	2	1	3
Percentage	61	33	30	0	38	40	9	18
Squamous cell carcinoma	5	6	21	12	18	5	6	15
5 Year survival	0	2	5	0	5	1	0	1
Percentage	0	33	24	0	28	20	0	6
Undifferentiated carcinoma	12	29	42	25	25	6	31	46
5 Year survival	6	8	9	2	8	2	7	8
Percentage	50	28	21	8	32	33	22	17

5 Year survival is actual number of patients living, not percentage.

TABLE XIX

5 YEAR SURVIVAL ACCORDING TO INVASION AREAS

	1	3	4	5	6B	7A	7D	8	9	No Area
Total	25	43	36	1	4	17	9	1	2	55
5 Year survival	2	10	6	1	1	0	2	0	0	16
Percentage	8	23	17	100	25	0	22	0	0	29
Male	16	31	21	1	3	9	7	1	2	41
5 Year survival	1	6	4	1	1	0	2	0	0	11
Percentage	6	19	19	100	33	0	29	0	0	24
Female	9	12	15	0	1	8	2	0	0	15
5 Year survival	1	4	2	0	0	0	0	0	0	5
Percentage	11	33	13	0	0	0	0	0	0	30
Squamous cell carcinoma	12	12	12	0	0	7	2	1	1	11
5 Year survival	0	5	1	0	0	0	0	0	0	2
Percentage	0	42	8	0	0	0	0	0	0	18
Undifferentiated carcinoma	13	31	24	1	4	10	7	0	1	45
5 Year survival	2	5	5	1	1	0	2	0	0	14
Percentage	15	16	21	100	25	0	29	0	0	31

1—Superior spread to base of skull; 3—inferior spread to oropharynx; 4—anterior spread to nose; 5—posterolateral spread; 6B—oribital and extracranial spread; 7A—parapharyngeal, prestyloid and anterior spread; 7D—parapharyngeal and retrostyloid spread; 8—hypophyseosphenoidal spread; 9—retrosphenoidal spread.

5 Year survival is actual number of patients living, not percentage.

DISTRIBUTION OF 5 YEAR CRUDE SURVIVAL ACCORDING TO STAGE RELATED TO LYMPH NODE INVOLVEMENT

This is shown in Table xx, where it is seen in Stage T_1 N_0 that 66 per cent of the cases survived 5 years, which is in accordance with other series, and that the results were better if the tumor was undifferentiated. These survival rates remained high even for tumors in Stage T_1 with bilateral mobile lymph nodes, especially if the tumor was undifferentiated. The survival rate dropped to 11 per cent with N_3. In Stage T_2 the survival rate with N_0 dropped to 40 per cent, but it remained high even for N_1 and N_2 and dropped to 7 per cent for N_3. In Stage T_3 N_0 the survival rate was still 40 per cent, but dropped with increasing lymph node involvement. In Stage T_4 there was practically no survival even without lymph node involvement. The results of this correlation between Stage and lymph node involvement leads us to conclude that Stage is more important for the cure and prognosis than lymph node involvement. The patients with carcinoma in T_1 and T_2 have better chance for cure, while those in T_4 have none, the chances being higher if the tumor is undifferentiated.

SUMMARY

1. A series of 152 patients with primary nasopharyngeal cancer from the Head and Neck Unit of the Royal Marsden Hospital was analyzed and the natural behavior of their tumors studied. The ratio of male to female was 2.1:1. The ratio of undifferentiated carcinoma to squamous cell carcinoma was 2.4:1. The ratio of male squamous cell carcinoma to female squamous cell carcinoma was 1.9:1. The ratio of male undifferentiated carcinoma to female undifferentiated carcinoma was 2.2:1. The ratio of male undifferentiated carcinoma to male squamous cell carcinoma was

TABLE XX

5 YEAR SURVIVAL ACCORDING TO STAGE RELATED TO LYMPH NODE INVOLVEMENT

	N_0	N_1	N_2	N_3
Stage T_1 total	3	—	5	9
5 Year survival	2	—	3	1
Percentage	66	—	60	11
Squamous cell carcinoma	1	—	1	3
5 Year survival	0	—	0	0
Percentage	0	—	0	0
Undifferentiated carcinoma	2	—	4	6
5 Year survival	2	—	3	1
Percentage	100	—	75	17
Stage T_2 total	10	3	8	14
5 Year survival	4	2	3	1
Percentage	40	66	37	7
Squamous cell carcinoma	2	—	—	4
5 Year survival	2	—	—	0
Percentage	100	—	—	0
Undifferentiated carcinoma	8	3	8	10
5 Year survival	2	2	3	1
Percentage	25	66	37	10
Stage T_3 total	17	5	16	24
5 Year survival	7	1	1	5
Percentage	41	20	6	20
Squamous cell carcinoma	11	3	3	3
5 Year survival	3	1	0	1
Percentage	27	33	0	33
Undifferentiated carcinoma	6	2	13	21
5 Year survival	4	0	1	4
Percentage	66	0	7	19
Stage T_4 total	13	3	8	13
5 Year survival	0	0	0	2
Percentage	0	0	0	15
Squamous cell carcinoma	4	2	2	4
5 Year survival	0	0	0	0
Percentage	0	0	0	0
Undifferentiated carcinoma	9	1	6	9
5 Year survival	0	0	0	2
Percentage	0	0	0	22

5 Year survival is actual number of patients living, not percentage.

2.5:1. The ratio of female undifferentiated carcinoma to female squamous cell carcinoma was 2.3:1.

2. The peak incidence was in the fifth and sixth decades, but the peak survival rate was in the fourth decade, females having a higher survival rate than males and patients with undifferentiated carcinoma having a higher survival rate than patients with squamous cell carcinoma. No patient in the first or second decade survived.

3. The most frequent initial site was the posterosuperior wall in which also the lowest survival rate was noted.

4. The most frequent presenting symptoms were nasal and auricular, with no relationship to the survival rate.

5. Dividing the patients into 5 groups based on the delay of diagnosis in months, the highest incidence was found in Group 0 to 6 months. Correlating the delay with Stage, to obtain the relationship between time-delay and local extent of the tumor—a factor which the writer calls clinical age of the tumor—it is shown that T_1 tumors have the highest proportion with 3 to 6 months delay, perhaps reflecting that they are rapidly growing and thus cause earlier symptoms. The tumors of T_2 and T_3 are more or less evenly distributed in all the delayed groups, perhaps reflecting an average growth pattern. Tumors T_4 show a slight tendency towards a greater time-delay, possibly reflecting a very slow tumor growth pattern. When we correlate this stage-delay relationship with the 5 year crude survival, we obtain the lowest survival rate in the 0 to 3 month delay group and the peak in the 6 to 9 month delay group, remaining rather stable for the 9 to 12 and more than 12 month delay groups. Based on these criteria of the clinical age of the tumor, the cases in this series may be considered as having 3 kinds of tumors:

a. Small tumors giving symptoms early and leading to demise of the patient rapidly;
b. tumors with an average growth pattern, giving symptoms later and producing a longer survival; and
c. tumors having a very slow growth pattern and thus producing a considerably longer survival.

6. Undifferentiated carcinomas showed a higher 5 year crude survival rate than squamous cell carcinomas, almost three times as high.

7. The peak incidence was in T_3 tumors

and the highest survival rate was in T_1. Based on lymph node involvement the highest survival rate was in N_0 tumors. Thus there was a close relationship between Stage, lymph node involvement and survival rate. Lymph node involvement, either bilateral or fixed, was present in 71.6 per cent of the patients.

8. The most frequently invaded areas were the oropharynx and nasal cavity, followed by spread superiorly to the base of the skull and the anterior prestyloid and retrostyloid parapharyngeal compartments. Tumors of the posterosuperior wall spread more frequently to the base of the skull. It is, therefore, advisable that the base of the skull, the posterior third of the nasal cavity, and a good portion of the oropharynx be included in the field when treating the primary tumor so as to cope with the possible spread to these areas, where it escapes us many times because of its submucosal infiltrating character. The patients with tumors spreading to the base of the skull had the lowest survival rate.

This series of cases was treated almost entirely with orthovoltage and therefore is not comparable to modern series treated with supervoltage.

Department of Radiation Therapy
Michael Reese Hospital and Medical Center
Chicago, Illinois 60616.

I would like to express my gratitude to Dr. M. Lederman, for his help and advice in the preparation of this paper.

REFERENCES

1. ACKERMAN, L. V., and DEL REGATO, J. A. Cancer: Diagnosis, Treatment, and Prognosis. Third edition. C. V. Mosby Company, St. Louis, 1962.
2. BACLESSE, F., and DULAC, G. Les tumeurs malignes du rhinopharynx: résultats éloignés de leur traitement par les radiations. *Bull. Assoc. franç. p. l'étude du cancer*, 1943, *31*, 16–177.
3. FLATMAN, G. E. Cranial nerve involvement by tumours of nasopharynx. *Proc. Roy. Soc. Med.*, 1954, *47*, 555–558.
4. FLETCHER, G. H., and MILLION, R. R. Malignant tumors of nasopharynx. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1965, *93*, 44–55.
5. GIGNOUX, M., and LABAYLE, J. Tumeurs de l'ethmoide. Masson & Cie, Paris, 1954.
6. GODTFREDSON, E. Ophthalmologic and Neurologic Symptoms of Malignant Nasopharyngeal Tumours. Ejnar Munksgaards Forlag, København, 1944.
7. GODTFREDSON, E., and LEDERMAN, M. Diagnostic and prognostic roles of ophthalmoneurologic signs and symptoms in malignant nasopharyngeal tumors. *Am. J. Ophth.*, 1965, *59*, 1063–1069.
8. LAMBERT, H., SNELLING, M., and FLATMAN, G. E. Discussion on treatment of carcinoma of nasopharynx. *Proc. Roy. Soc. Med.*, 1954, *47*, 547–560.
9. LEDERMAN, M. Cancer of the Nasopharynx, Its Natural History and Treatment. Charles C Thomas, Publisher, Springfield, Ill., 1961.
10. LEDERMAN, M. Cancer of nasopharynx. *Proc. Roy. Soc. Med.*, 1964, *57*, 740–742.
11. RINGERTZ, W. Pathology of malignant tumours arising in nasal and paranasal cavities and maxilla. *Acta Oto-laryng.*, 1938, Suppl. 27.
12. SCANLON, P. W., DEVINE, K. D., and WOOLNER, L. B. Malignant lesions of nasopharynx. *Ann. Otol., Rhin. & Laryng.*, 1958, *67*, 1005–1021.
13. SCANLON, P. W., RHODES, R. E., JR., WOOLNER, L. B., DEVINE, K. D., and MCBEAN, J. B. Cancer of nasopharynx: 142 patients treated in eleven year period 1950–1960. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1967, *99*, 313–325.
14. SMEDAL, M. I., and WATSON, J. R. Treatment of cancer of nasopharynx with two million volt radiation. *S. Clin. North America*, 1959, *39*, 669–675.
15. TERRACOL, J., CORONE, A., and GUERRIER, Y. La Trompe de'Eustache. Masson & Cie, Paris, 1949.
16. VAETH, J. M. Nasopharyngeal malignant tumors: 82 consecutive patients treated in period of twenty-two years. *Radiology*, 1960, *74*, 364–372.
17. WANG, C. C., LITTLE, J. B., and SCHULZ, M. D. Cancer of nasopharynx: its clinical and radiotherapeutic considerations. *Cancer*, 1962, *15*, 921–926.
18. WANG, C. C., and SCHULZ, M. D. Management of locally recurrent carcinoma of nasopharynx. *Radiology*, 1966, *86*, 900–903.
19. WINDEYER, B. W., and SMITHERS, D. W. Tumors of nose and nasal sinuses. In: British Practice in Radiotherapy. Butterworth & Company, London, 1955, pp. 208–226

RADIATION THERAPY OF CARCINOMA OF THE ANTERIOR NASAL CAVITY*

By WAYNE P. WHITCOMB, M.D.†
NEW HAVEN, CONNECTICUT

TEXTBOOKS on radiation therapy comment but briefly upon the treatment of malignant lesions of the anterior nasal septal mucosa and adjacent vestibule. Among British authors Paterson,[8] Cade,[3] and Carling *et al.*[4] make mention of these lesions but only Cade goes into detail. Murphy[7] has discussed the subject in his American textbook. A review of the radiologic literature reveals few articles[1,9] touching on similar lesions. When anterior nasal lesions are mentioned, the impression is gained that the prognosis following radiation therapy is good to excellent and that the entity is rare compared to other lesions of the nasal cavity, nasopharynx, and accessory sinuses. The paucity of information on the subject prompts this report.

The anatomy of the area is such that it presents problems of radioimplantation, both of technique and potential complication. Technique is difficult because of the irregular shape of the nasal cavity and because of the thin tissue into which the implant is made. The threat of the radiotherapeutic complication of necrosis is real because of the immediate proximity of cartilage and bone to the implanted mucosa and epidermis. Due to the peculiar shape of the nose, difficulties of needle placement and dosage assessment increase the probability of local high dosage and subsequent complications. The chronic irritation to which the thin nasal mucosa is subjected adds to the possibility of complications.

A review of the physiologic anatomy[2,5,6] of the area, both pre and post-therapy will be of some help in estimating the problem, determining treatment, and in establishing follow-up routine.

ANATOMY

The nose is the initial organ of respiration. There air, entering, is warmed and partially filtered of impurities by fine epidermal hairs extending just within the external nares (vestibule). Definitive radiation therapy will result in a loss of these hairs and their function, permitting the admission of cold air and larger quantities of impurities into the nasal cavity. Posteriorly and above the vestibular epidermis, the nasal cavity is lined with a mucous membrane relatively closely applied to the bones and cartilage of the nose. This mucous membrane consists of a pseudosquamous ciliated columnar epithelium containing many acinous glands and a very rich vascular plexus. The mucous membrane is quite sticky, causing dust to adhere; thus the membrane acts as another trap for airborn impurities. The normal cilia, by a beating motion, tend to move the secretions and trapped impurities out of the nose. Curative irradiation will destroy the cilia and the glandular function, leading to post-treatment encrustation of the anterior nasal lining. Fortunately, the therapeutic ratio of tumor to mucosa is enhanced by the rich blood supply.

The venous drainage of the anterior respiratory mucosa and its venous plexus is to the anterior facial vein forwards; into the ethmoidal vein superiorly; and into the sphenopalatine vein posteriorly. Numerous arteriovenous communications (erectile tissue) are also present.

The lymph vessels of the external nose and anterior cavity of the nose drain to the submandibular lymph nodes. The remainder of the cavity drains to the upper deep

* From the Radiation Therapy Center, The Hospital of St. Raphael, New Haven, Connecticut.
† Clinical Associate in Radiology, Yale University School of Medicine; Director, Radiation Therapy Center, Hospital of St. Raphael.

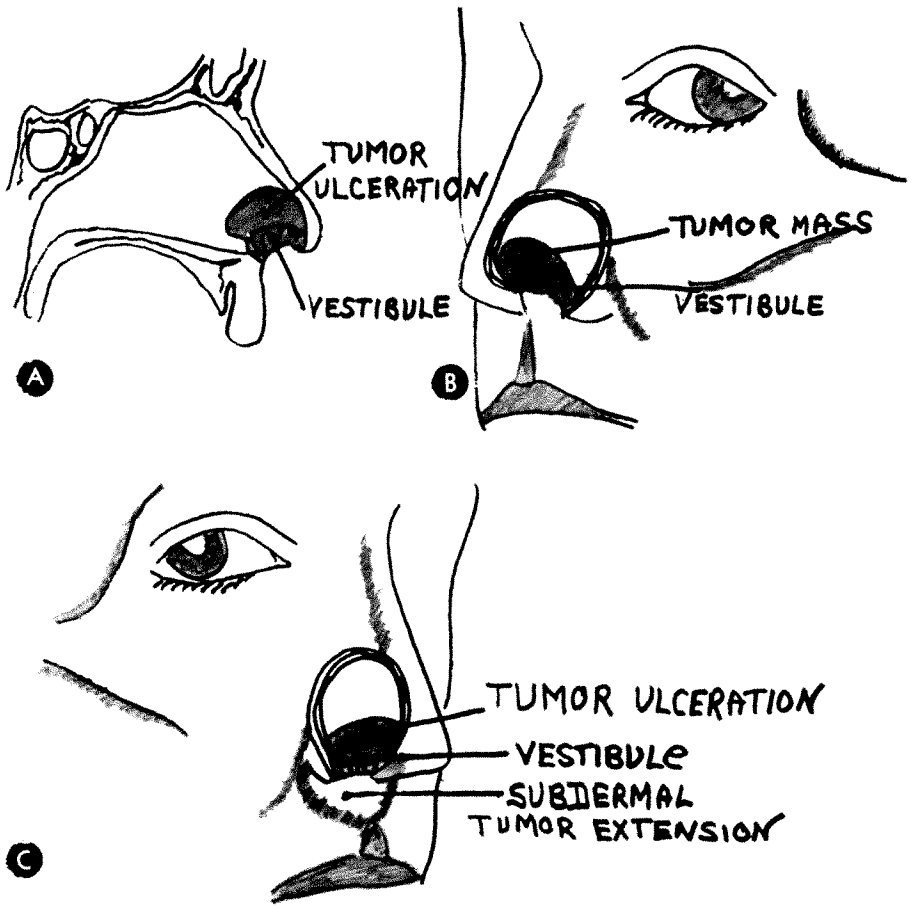


Fig. 1. Diagrams of tumor location. (*A*) Case I. (*B*) Case II. (*C*) Case III.

cervical chain, possibly through a retropharyngeal lymph node, save for the posterior floor which drains to the parotid lymph nodes.

At the Radiation Therapy Center of the Hospital of St. Raphael, we have recognized but 3 primary tumors of the anterior nasal septum and vestibule in the period from January, 1948, through May, 1966. During that same period we have treated 3,919 malignancies of all kinds and 375 malignancies considered to arise within the nose, accessory sinuses, mouth, pharynx, and larynx (exclusive of lip and salivary gland tumors). Thus these 3 cases represented only 0.08 per cent of our total tumor load and only 0.8 per cent of tumors of the nose, accessory sinuses, mouth, pharynx, and larynx seen by us.

REPORT OF CASES

Case I. L. Van H., 45 year old white male executive underwent radium implantation on January 20, 1954. He gave a history of having cut himself about 1 year previously inside the nose when clipping vestibular hair. The cut failed to heal so that he consulted an otolaryngologist in November, 1953, who treated the lesion conservatively and when healing did not occur, performed a biopsy on January 15, 1954. The lesion proved to be an epidermoid carcinoma, Grade II. The patient was referred for radiation therapy. The lesion physically was a shallow ulceration of the anteroinferior aspect of the right side of the septum, probably arising from the septum near the mucocutaneous junction and extending laterally onto the floor of the right nare (Fig. 1*A*).

The lesion was implanted with 5 needles of 2 cm. active length directed posteriorly and

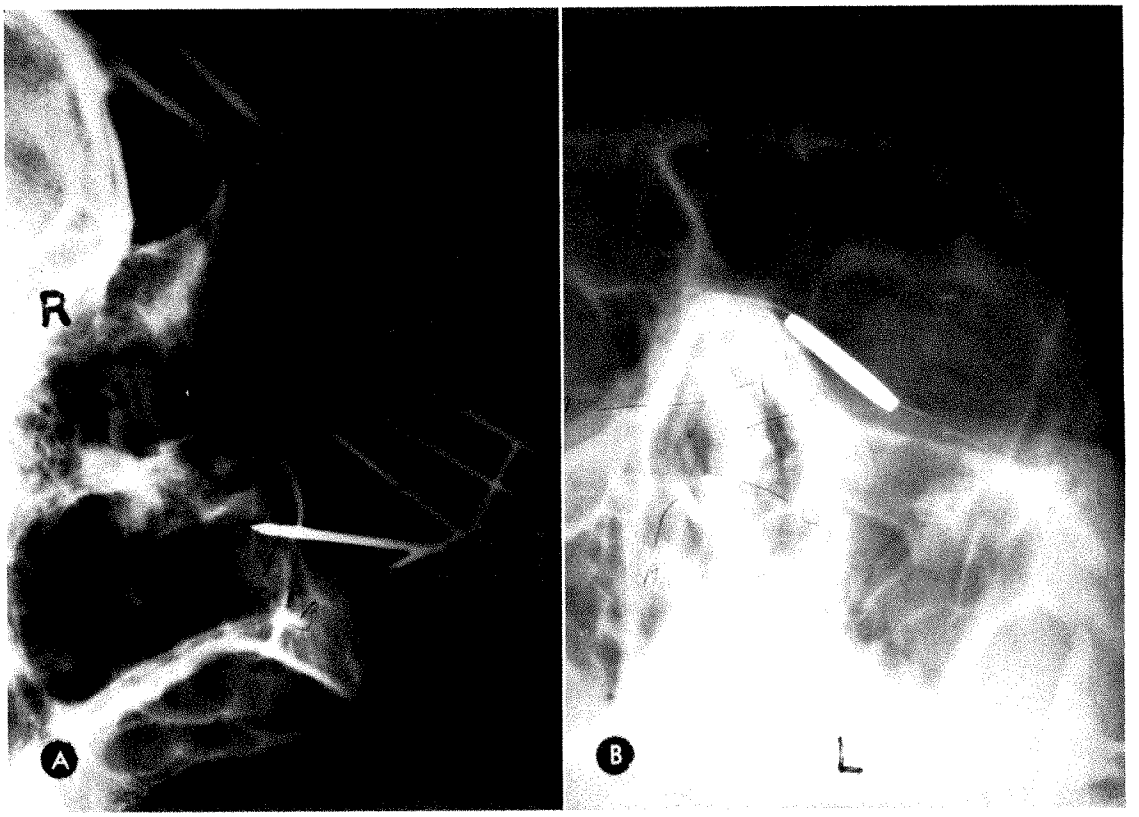


Fig. 2. Case 1. (*A* and *B*) Roentgenograms of radium needle implants.

roughly parallel to each other along the septum and right floor of the nose (Fig. 2, *A* and *B*). The most superior and most lateral of these needles were of 0.75 mg./cm. activity and the 3 intermediate needles of 0.5 mg./cm. One centimeter active length needles of 0.5 mg./cm. activity were crossed through the dermal covered soft tissues of the free edge of the septum and the anterior edge of the right floor of the nose adjacent. The estimated area of this "L" shaped folded planar implant was taken as 5 cm.^{2} and an estimated dose (Manchester method) of 6,760 rads given in 157 hours. By April 23, 1954 complete healing had occurred.

The patient was seen again on April 28, 1966, with an infected ulceration of the right septum successfully treated by Bacitracin and the advent of warmer weather. He was well when last seen on September 22, 1967.

Case II. G. G., a 69 year old white male, underwent radium implantation here January 11, 1958, upon referral from the tumor clinic of this hospital. He gave a history of recurrent nose bleeds, over a period of 1 year. In August, 1957, the patient noted "tissue growth" in the left vestibule which persisted and enlarged. Two weeks before initial presentation, the area had become sensitive and sore. He was seen at the Tumor Clinic for examination; a biopsy performed on January 3, 1958, showed epidermoid carcinoma, Grade II. Physical examination revealed a soft tissue mass situated medially in the left vestibule, the mass extending along the septum both superiorly and posteriorly (Fig. 1*B*). The tumor dimensions were 2.5 $\times$0.5 cm. The lesion was of very firm consistency upon palpation. The radium implant was similar to that of Case 1, except that the crossing needles were of 0.75 mg./cm. linear activity (Fig. 3, *A* and *B*). The final implantation area was estimated to be 6 cm.^{2}. A dose of 6,000 r was given in 160 hours. The area had completely healed with a minimum of scarring by March 25, 1958, and has remained healed as of July 18, 1967. The dose in this case was lowered due to our experience with Case 1, in which we thought the radiation reaction unnecessarily severe. The external cosmetic result in both cases has been quite satisfactory.

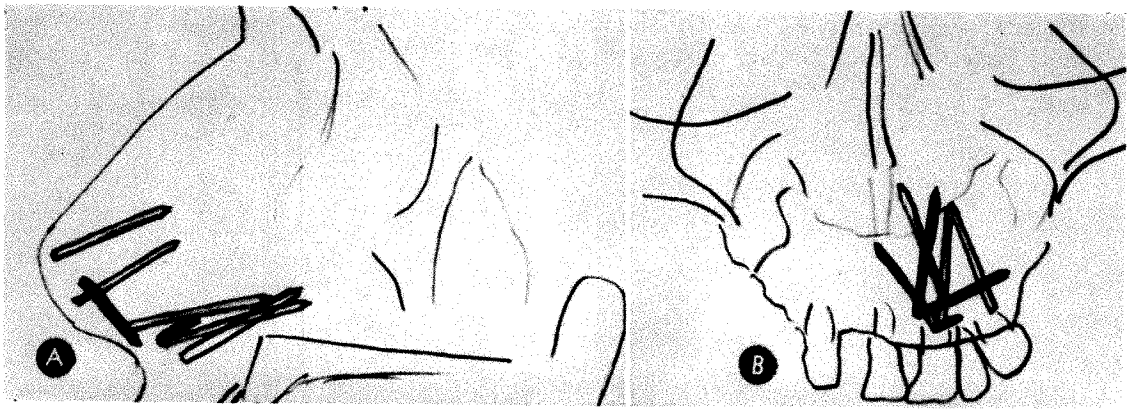


FIG. 3. Case II. (*A* and *B*) Tracing from roentgenograms of radium needle implants.

Comment. These 2 implantations were done under general anesthesia through a peroral intratracheal tube with a pharyngeal pack to prevent aspiration of blood and other matter. After making preliminary tiny stab incisions of the skin, needles were passed through the external edge of the septum, roughly parallel to the floor of the nose and into the mucosa along the bony-cartilagenous septum on the side of the lesion; also into the floor of the nose in similar way. The needle at the junction of the septum and floor served as the hinge of the "L" shaped implants. Crossing needles were passed along the dermal edge of the septum and the floor of the nose. All needles were individually sutured in place on the external nose by small silk sutures passed through a bight made of the larger, longer silk sutures at the eye of the needle. The large sutures, which pass through the eye of the radium needles, were then twisted together, brought around the ear and taped against the cheek.

CASE III. J. H., a white male aged 59 years, presented for first treatment on July 22, 1963, with a history of having had an object lodge in the right nostril during an industrial accident 6 months previously. After removal, delayed healing occurred and the patient was referred by his internist to an otolaryngologist who then referred the patient for radiation therapy after a biopsy showed epidermoid carcinoma, Grade III.

On physical examination there was an ulceration of the right vestibule at the angle between the septum and the floor extending upwards onto the septum, but with induration extending downward below the floor of the nostril into the deeper tissues of the upper lip, one-half the distance to the vermillion border of the lip from the nasal introitus (Fig. 1*C*).

Because of the downward extension it was decided to treat this patient by a single external 5 cm. diameter, deep x-ray field compressed against the right side of the nose and subjacent tumor extension. At a half value layer of 2.25 mm. Cu and 50 cm. target-skin distance, a maximum skin dose of 4,995 rads with a minimum tumor dose of 4,875 rads was delivered in 19 days in 15 equally divided treatments. A marked, exudative, crusting reaction ensued with nearly complete healing by September 6, 1963. Slight rawness of the septal area remained for about 1 additional year. As of October 13, 1967, the patient presented healed except for occasional periodic crusting in the area.

Comment: Radium implantation of tumors of the vestibule and anterior nasal septum is quite feasible and results in no more post-therapeutic morbidity than is encountered elsewhere in the body as long as ordinary dose limits are used. We have felt that where the tumor is larger than 2.5 to 3.0 cm. in greatest diameter, external radiation therapy is probably the better mode of treatment.

SUMMARY

The physiology and anatomy of the anterior nasal septum and vestibule are discussed.

Three cases of primary tumors of the anterior nasal septum and adjacent vestibule septum are reported: 2 were treated by radium implantation and are alive and free of disease at 13 and 9 years, respectively; and 1 was treated by deep roentgen-ray therapy and is alive and well at 4 years.

The 3 cases represented 0.1 per cent of the total tumor load and 1.0 per cent of specified nose and throat cases at the Radiation Therapy Center of the Hospital of St. Raphael.

Radiation Therapy Center
Hospital of St. Raphael
New Haven, Connecticut 06511

REFERENCES

1. BRADDON, P. D. Sandwich radium moulds applied to nasal neoplasms. Year Book of Radiology, 1943, p. 392. *Australian & New Zealand J. Surg.*, 1942, *12*, 149–151.
2. BEST, C. N., and TAYLOR, N. B. The Physiological Basis of Medical Practice. Third edition. Williams & Wilkins Company, Baltimore, 1943, pp. 491–493.
3. CADE, S. Malignant Disease and Its Treatment by Radium. Volume II. Second edition. Williams & Wilkins Company, Baltimore, 1949, pp. 184–197.
4. CARLING, E. R., WINDEYER, B. W., and SMITHERS, D. W. Practice in Radiotherapy. C. V. Mosby Company, St. Louis, 1955, pp. 208–210.
5. GRAY, H. Anatomy of the Human Body. Twenty-fourth edition. Edited by W. H. Lewis. Lea & Febiger, Philadelphia, 1942, pp. 139–141 and 1010–1016.
6. LOCKHART, R. D., HAMILTON, G. F., and FYFE, F. W. Anatomy of the Human Body. J. B. Lippincott Company, Philadelphia, 1959, pp. 477–480.
7. MURPHY, W. T. Radiation Therapy. Second edition. W. B. Saunders Company, Philadelphia, 1967, pp. 293–299.
8. PATERSON, R. Treatment of Malignant Disease by Radiotherapy. Second edition. Williams & Wilkins Company, Baltimore, 1963, p. 261.
9. VIEIRA, A. P. Radiotherapy of Malignant Tumors of Nasal Fossa. Year Book of Radiology, 1957–58, pp. 274–275. *Rev. brasil. cir.*, 1956, *32*, 491–504.

VOL. 105, NO. 3

HYDROXYUREA: A RADIOSENSITIZER IN THE TREATMENT OF NEOPLASMS OF THE HEAD AND NECK*

By GEORGE J. RICHARDS, JR., M.D.,† *and* ROBERT G. CHAMBERS, M.D.‡
BALTIMORE, MARYLAND

FOR a number of years radiation therapists have sought a radiosensitizing substance which would enhance the effect of ionizing irradiation on malignant cells. Many agents have been used with limited effectiveness. Previous efforts have centered about the limited knowledge of the biologic effects of ionizing irradiation on the malignant cell.

The enhancement of the radiation effect by increased oxygen saturation of the malignant cell led to the development of the Hyperbaric Chamber and the local infusion of peroxidase. The knowledge that actively dividing cells are more radiosensitive than resting cells led to attempts to stimulate mitotic activity by means of various hormones and known cell stimulants. Attempts have been made to alter cellular metabolism by either speeding up metabolic activity, as in the case of thyroxin, or producing injury or death concomitant with radiation effect, as in the case of antimetabolites and alkalating agents. The results of treatment of epidermoid carcinomas of the head and neck, even after radical surgery and extensive radiotherapy, have been poor. Attempts to improve the results have included extensive use of chemotherapeutic agents used either concomitantly with radiotherapy or prior to radiotherapy, intra-arterial infusion of a chemotherapeutic agent, preoperative irradiation and postoperative irradiation. These have contributed slightly to an increased statistical salvage rate in this area. It has long been noted that the radiosensitivity of cells undergoing division is not uniformly increased over the entire mitotic cycle. It is generally considered that the stage of the equatorial plate is the most sensitive phase (G_1 or G_2). Thus, an ideal radiosensitizing agent would be one which could destroy relatively radioresistant cells in the S stage and synchronize other cells in a relatively radiosensitive stage (G_1 or G_2), permitting irradiation to be more effective. Hydroxyurea has been proposed as such an agent.

At the Greater Baltimore Medical Center, an extensive study as to the radiosensitizing properties of Hydroxyurea* in the treatment of neoplasms of the head and neck was conducted. Patients presenting with primary untreated neoplasms of the head and neck were randomized into groups in a double blind study, 1 group receiving Hydroxyurea, the second group an identical placebo capsule. The drug was administered intermittently, 80 mg. per kg. body weight, given in a single oral dose every third day. Simultaneously, therapeutic irradiation was given over a period of 3 to 10 weeks. Upon completion of the irradiation, Hydroxyurea was continued and approximately 6 to 8 weeks following the completion of irradiation, multiple biopsies and more definite surgery where indicated were performed. A comparison of clinical regression and pathologic response was made between the 2 groups. A third group of patients, with tumor recurrences or failure to respond to previous surgery and/or

* Hydrea, Squibb.

* Presented at the Fiftieth Annual Meeting of the American Radium Society, Miami Beach, Florida, April 7–11, 1968.
From the Department of Radiology and the Division of Head and Neck Surgery, Department of Otolaryngology, Greater Baltimore Medical Center, Baltimore, Maryland.
† Chief of Radiology, Greater Baltimore Medical Center; Assistant Professor of Radiology, The Johns Hopkins University, Baltimore Maryland.
‡ Chief, Division of Head and Neck Surgery, Greater Baltimore Medical Center; Assistant Professor of Surgery, The Johns Hopkins University, Baltimore, Maryland.

irradiation, were treated with Hydroxyurea and irradiation and the effectiveness of their response evaluated.

CRITERIA FOR CLINICAL EVALUATION

Each patient was evaluated for subjective and objective responses to the concomitant radiation-Hydroxyurea therapy. The various subjective and objective findings were noted as follows (Tables I and II):

1. Patient identification was the initial of the first and last name, together with the patient's age and sex.

2. Location: the primary site of the tumor, where the origin was easily identified, was listed. In an extensive tumor of the hypopharynx and larynx, it was frequently difficult to designate the specific location within these larger anatomic regions. Occasionally the technique of designating the primary site as the last area of tumor regression to radiation therapy was utilized.

3. Clinical staging was based upon the classification recommended by the International Committee for Stage-grouping in Cancer as follows:

I. Staging of Primary Tumor
- T_1 Less than 3 cm. in diameter
- T_2 3 to 5 cm. with minimal extension into adjacent tissues
- T_3 Greater than 5 cm. with limited extension into adjacent structures
- T_4 Massive local invasion

II. Staging of Lymph Node Metastasis
- N_0 No lymph node
- N_1 Single, small to moderate size (less than 3 cm.)
- N_2 Large, movable lymph node or multiple unilateral lymph nodes, (more than 2 cm.)
- N_3 Fixed, large unilateral lymph node or bilateral lymph nodes, (more than 2 cm.)

III. M Distant metastases when first seen.

4. Pathologic findings: this column contains a description of (a) the pretreatment biopsy pathologic report, and (b) the post-treatment surgical specimen report. In both of these, the microscopic description contained the predominant cellular type and the degree of differentiation of the cellular type. It also included the extent of lymph node involvement. Post-treatment specimens also described the extent of necrosis and radiation response.

5. Hydroxyurea therapy: all patients received a dose of 80 mg. per kg. of body weight administered on every third day orally. This column describes the total dosage of Hydroxyurea and the total number of days over which the drug was administered.

6. Concomitant therapy: all of these patients were treated with a Theratron 80, cobalt 60 source with fixed fields. The fields were designed to include the primary site of treatment and the additional regional involvement. The entire lymph node areas were not prophylactically treated unless there were definite signs of clinical involvement. This column gives the total number of rads and the days over which the dosage was administered.

7. Surgery: this column indicates the extent of surgery performed, both as to the primary site and the regional lymphatics.

8. Complications: this column records the toxicity. Some of these symptoms are due to the drug therapy; others can be attributed to irradiation and some most certainly are a combined effect of both modalities.

9. Results: a summation of response and follow-up data is reported. The patients were divided into 3 groups. Groups I and II represented a double blind study in which patients were selected at random irrespective of location, clinical staging, pathologic findings, or age and sex. They were selected entirely at random by a nurse member of the research team who had no knowledge as to the disease of the patient. These patients received identical capsules, one of which was designated JMG, the other designated JMH. At the time of the completion of this current study, the coded envelopes were

broken and it was detected that JMG was the placebo and JMH was in fact Hydroxyurea. Group III received irradiation and Hydroxyurea therapy. These patients represented individuals who had suffered recurrences from previous modalities of therapy, either surgery or irradiation or both. In other cases, they represented patients with distant metastases when first seen.

RESULTS

There were 20 patients in each randomized group. Group I was treated with placebo and irradiation (Table I). Group II was treated with Hydroxyurea and irradiation (Table II).

AGE AND SEX

In Group I there were 13 males and 7 females with a mean age of 56 years. There were 9 males and 11 females in Group II with a mean age of 53 years.

LOCATION OF PRIMARY TUMOR

The location of the primary tumor was as follows:

	Group I	Group II
Tongue	5	3
Floor of Mouth	4	2
Tonsil	2	2
Nasopharynx	1	1
Palate	1	1
Larynx	5	4
Hypopharynx	1	3
Nose	—	1
Parotid	1	2
Maxillary sinus	—	1

CLINICAL STAGING

In Group I primary tumors were staged as follows: T_1 (2), T_2 (3), T_3 (5), and T_4 (9). Twelve had lymph node involvement at the time they were originally seen. In Group II staging was as follows: T_1 (4), T_2 (6), T_3 (3), and T_4 (7). Eight patients had clinically palpable lymph nodes.

RADIATION THERAPY

Time-dose relationships and factors of irradiation were comparable. All patients in both groups were treated with a Theratron 80, cobalt 60 unit with a 2 cm. source and fixed fields. The fields of irradiation included the primary tumor with its local extension and involved lymph nodes. Fractionation and gentleness were practiced where possible. Time-dose relationships were recorded as follows: 4,000–6,000 rads in 21–36 days, Group I (3), Group II (5); 5,000–7,000 rads in 42–56 days, Group I (10), Group II (10); 6,000–9,000 rads in 56–84 days, Group I (7), Group II (5).

DRUG THERAPY

All patients in both groups received identical appearing capsules. Each was assumed to contain 500 mg. of the drug. Each patient received an equivalent of 80 mg. per kg. of body weight orally every third day. Upon the completion of the data compilation, the code was broken revealing that Group II had received Hydroxyurea. The total amount of drug received by patients varied from 20 to 350 gm. administered over a range of 15 to 206 days.

SURGICAL PROCEDURE

In Group I, 12 patients underwent radical excisions of the primary tumor; 13 had radical neck dissections; 2 had multiple biopsies; and 6 had no post-treatment surgery. Radical surgical excision of the primary tumor was done in 11 cases in Group II. Eleven had radical neck dissections, 1 had a biopsy and 8 had no post-treatment surgery.

PATHOLOGIC FINDINGS

In Group I, of 12 operative cases, 6 had viable cells in the primary site, 2 were negative and 4 were positive for tumor, but had a noticeable radiation effect. Lymph node studies revealed 6 with positive lymph nodes, 1 positive with irradiation effect and 5 negative for tumor.

In Group II, analysis of the primary site revealed viable tumor in 4 cases, 6 were negative and 1 was positive with radiation effect. All 11 patients presented negative lymphadenectomies.

TABLE I

SUMMARY OF PATIENTS TREATED WITH PLACEBO AND IRRADIATION CONCOMITANTLY

Patient	Age (yr.)	Sex	Location of Primary Tumor	Clinical Stage	Pathologic Type	Total Radiation Dosage (rads/days)	Surgery		Complications	Results
							Procedure	Pathologic Findings		
J.G.	51	M	Larynx, subglottic	T_2N_0	Poorly differentiated squamous cell carcinoma	6,000/35	Total laryngectomy; bilateral radical neck dissection	Massive radiation reaction; foci of radiate squamous cells throughout negative lymph nodes	Postoperative submental fistula	Tumor present in specimen; margins free; 100 per cent—7 months
P.G.	59	M	Tongue, floor of mouth	T_2N_0	Differentiated squamous cell carcinoma	8,100/119	Hemiglossectomy; radical neck dissection	Differentiated squamous cell carcinoma in tongue; 33 negative lymph nodes	None	Marked regression of primary lesion but a 3 cm. mass present in tongue (viable tumor); good margins; 100 per cent—3 months
E.G.	40	F	Alveolar ridge, floor of mouth	T_2N_1	Well differentiated squamous cell carcinoma	6,000/51	Composite with radical neck dissection	Small foci of radiation-treated squamous cell carcinoma in primary site; 23 negative lymph nodes	None	Persistent tumor in specimen; margins free; 100 per cent—7 months
D.F	58	M	Alveolar ridge, floor of mouth	T_1N_0	Well differentiated squamous cell carcinoma	6,600/45	No post-treatment (pretreatment—local excision)	None	None	7 months—100 per cent tumor free
A.C.	60	F	Palate	T_1N_0	Well differentiated squamous cell carcinoma	6,000/47	Radical resection of palate	No malignancy	None	100 per cent tumor free at time of surgery
J.C.	47	M	Larynx, vocal cord and supraglottic	T_2N_0	Differentiated squamous cell carcinoma	4,000/37	Laryngectomy; bilateral neck dissection	Carcinoma cells in larynx, vestibule, epiglottis; 1/41 lymph nodes positive	None	Extensive tumor in operative specimen; margins free; 100 per cent—4 months
E.S.	59	F	Tonsil	T_2N_2	Differentiated squamous cell carcinoma	6,000/58	Composite; radical neck dissection	Squamous cell carcinoma showing radiation effect in tonsilar fossa; lymph nodes negative	None	Failure to destroy completely the primary lesion but complete destruction of tumor in a 6 cm. lymph node. 100 per cent adequate margins
F.W.	59	M	Larynx, supraglottic, hypopharynx	T_2N_2	Poorly differentiated squamous cell carcinoma	6,200/48	Laryngectomy; radical neck dissection	Marked radiation reaction; primary lesion negative; 1/20 lymph nodes positive	Severe pharyngeal stenosis	Complete control of primary tumor; active disease in deep jugular lymph node; 100 per cent—7 months
W.B.	62	M	Tonsil hypopharynx	T_2N_2	Well differentiated squamous cell carcinoma	8,000/63	None	None	None	Marked regression of primary tumor but failure to regress in lymph nodes; patient died of cerebral causes 40 days after irradiation
L.B.	55	M	Nasopharynx	T_4N_2	Differentiated squamous cell carcinoma	7,000/66	None	None	Severe infection and post-radiation edema; leukopenia 7,100–3,000/17 days	100 per cent—9 months both primary lesion and lymph nodes

TABLE I (*Continued*)

Patient	Age (yr.)	Sex	Location of Primary Tumor	Clinical Stage	Pathologic Type	Total Radiation Dosage (rads/days)	Surgery		Complications	Results
							Procedure	Pathologic Findings		
C.B.	77	F	Parotid, (pulmonary metastases, recurrent neck)	M	Adenocarcinoma	Mediastinum 5,000/65; neck 5,000/36	None	None	Radiation pneumonitis	4 cm. postauricular mass-100 per cent regression; hilar lymph nodes and pulmonary lesion—60 per cent regression
W.G.	68	M	Base of tongue, hypopharynx, tonsil	T_4N_2	Anaplastic squamous cell carcinoma	9,000/99	Left radical neck dissection; biopsy of pharynx	No remaining tumor	None	No tumor at time of surgery; 3 months postsurgery-3 cm. mass in right supraclavicular fossa—squamous cell carcinoma
C.W.	71	M	Tongue, posterior 1/3	T_4N_2	Well differentiated squamous cell carcinoma	7,000/60	None	None	None	Primary site: complete disappearance. Lymph node: reduction 7 cm. to 3 cm.; 6 months follow-up (status as above)
A.S.	63	M	Tongue, floor of mouth	T_3N_3	Moderate differentiated squamous cell carcinoma	6,200/51	Composite; base of tongue; right neck dissection	Single nidus in tongue; 1/40 lymph nodes positive for squamous cell carcinoma	None	Persistent viable tumor at surgery both in primary site and lymph node; good margins; 100 per cent effective—7 months
O.R.	58	M	Larynx, subglottic	T_4N_0	Undifferentiated squamous cell carcinoma	6,000/55	Composite laryngectomy; bilateral radical neck dissection; partial esophagectomy	Primary: no tumor in larynx or pharynx, lymph nodes: 3/58 positive	None	Persistent tumor in lymph nodes; 100 per cent—4 months
S.I.	69	M	Larynx, subglottic, supraglottic, pyriform sinus	T_4N_0	Differentiated squamous cell carcinoma	4,200/23	Composite laryngectomy; bilateral radical neck dissection	Nests of squamous cells of ? viability at base of tongue; 2 lymph nodes positive for viable squamous cell carcinoma	3 months later metastasis to liver and periaortic lymph nodes; (poorly differentiated squamous cell carcinoma)	100 per cent eradication of tumor in neck but viable cells in specimen; patient died of metastases
M.H.	62	F	Epiglottis, vestibule	T_2N_3	Differentiated squamous cell carcinoma	7,000/59	Hemilaryngectomy; bilateral radical neck dissection	Extensive tumor in primary site and lymph nodes	None	Extensive viable tumor; good margins; 100 per cent—3 months
A.G.	47	F	Oropharynx, floor of mouth, recurrent (bilateral)	T_4N_2	Undifferentiated squamous cell carcinoma	6,700/98	4 months prior, radical neck dissection	Undifferentiated squamous cell carcinoma	Severe mucositis	Patient succumbed to overwhelming inanition and tumor; no tumor control at any time
M.C.	65	M	Larynx, subglottic, vallecula, cricoid	T_4N_0	Differentiated squamous cell carcinoma	7,000/93	Biopsy	Squamous cell carcinoma in larynx and tracheostomy site	None	Persistent tumor at surgery
S.O.	45	F	Floor of mouth, base of tongue	T_2N_0	Differentiated squamous cell carcinoma	7,200/68	Composite, neck dissection	No viable tumor; necrotic tumor in floor of mouth and 1 of 24 lymph nodes	None	100 per cent effective eradication

TABLE II

SUMMARY OF PATIENTS IN DOUBLE BLIND STUDY TREATED WITH HYDROXYUREA AND IRRADIATION CONCOMITANTLY

Patient	Age (yr.)	Sex	Location of Primary Tumor	Clinical Staging	Pathologic Type	Total Radiation Dosage (rads/days)	Total Drug Dosage (gm./days)	Surgery		Complications	Results
								Procedure	Pathologic Findings		
M.M.	65	F	Maxillary sinus and orbit	T_4N_0	Anaplastic squamous cell carcinoma	6,000/38	182/142	Radical right maxillectomy, antrectomy, eventration of orbit	Poorly differentiated squamous cell carcinoma with extensive necrosis and submucosal extension; margins clear	Leukopenia 2,000 Day 30; nausea and anorexia	Viable tumor at surgery; 100 per cent—7 months
G.L.	60	M	Larynx (glottis)	T_1N_0	Well differentiated squamous cell carcinoma	7,000/88	275/165	None	None	Leukopenia 6,100–2,500 Day 18; 1,950 Day 31; off drug 9 days; 5,000 Day 40; 2,000 Day 70; 5,000 Day 88	100 per cent—6 months
B.K.	52	F	Tongue, floor of mouth	T_2N_0	Moderately differentiated squamous cell carcinoma	4,500/21	36/36	Radical composite; left hemiglossectomy, mandibular resection, radical neck dissection	Well differentiated squamous cell carcinoma with marked radiation reaction; 17 lymph nodes negative; margins free	Mucocutaneous fistula	Surgery 22 days after completion of irradiation and hydrea; tumor present in primary site with extensive radiation effect; 100 per cent tumor free 6 months
L.K.	33	F	Parotid (recurrent)	T_1N_1	Adenocarcinoma, adenocystic	6,000/44	90/30	Previous radical parotidectomy with radical neck dissection	Posterior auricular nodule, 3 cm. (recurrent)	Nausea and vomiting; leukopenia 10,000 to 2,800 Day 18; 2,000 Day 30	Drug discontinued on Day 30; 100 per cent regression of nodule; 5 months tumor free
J.K.	62	M	Floor of mouth	T_2N_0	Well differentiated squamous cell carcinoma	7,000/62	162/71	Composite resection with radical neck dissection	Floor of mouth—no malignancy; 19 lymph nodes negative	Postoperative cerebrovascular accident with recovery	100 per cent tumor free at surgery
R.J.	69	M	Tongue, floor of mouth	T_2N_1	Differentiated squamous cell carcinoma (5 cm. lesion)	2,400/15	25/15	No surgery	None	Dead of a myocardial infarction on Day 16	100 per cent clinical regression in 16 days
A.G.	63	M	Nasopharynx	T_1N_2	Poorly differentiated squamous cell carcinoma	7,000/82	235/165	No surgery	None	Leukopenia 6,400 to 1,750 Day 24; 6 day rest; 3,600 Day 30; 2,000 Day 148; 6 day rest; 4,000 Day 154	100 per cent regression of large bilateral lymph nodes—6 months
L.G.	69	M	Larynx, hypopharynx (pyriform sinus)	T_2N_0	Well differentiated squamous cell carcinoma	3,500/34	42/84	Total laryngectomy, with bilateral neck dissection	Right vocal cord-squamous cell carcinoma, remaining larynx and pyriform sinus—negative; lymph nodes negative	Severe radiation epidermitis with necrosis of the epiglottis and vestibule	Preoperative irradiation 36 days: 80 per cent preoperative regression; tumor viable in primary site; 100 per cent—6 months
J.C.	61	M	Larynx (epiglottis, glottis)	T_2N_0	Well differentiated squamous cell carcinoma	5,500/45	75/57	Total laryngectomy with radical neck dissection	One focus of viable well differentiated squamous carcinoma cells at opposing margins of right true and false cords; large masses of necrotic cells; lymph nodes negative	Leukopenia 1,800 Day 30; 6 day rest; 3,000 Day 36	80 per cent preoperative regression; viable tumor in primary site
C.B.	52	M	Larynx (supraglottic and subglottic)	T_4N_0	Poorly differentiated squamous cell carcinoma	6,000/48	112/75	Laryngectomy with bilateral radical neck dissection	Larynx—no tumor; 16 lymph nodes—negative	Leukopenia: 7,500 to 1,850 Day 10; spontaneous recovery	100 per cent tumor free at surgery and 5 months

TABLE II (*Continued*)

Patient	Age (yr.)	Sex	Location of Primary Tumor	Clinical Staging	Pathologic Type	Total Radiation Dosage (rads/day)	Total Drug Dosage (gm./day)	Surgery		Complications	Results
								Procedure	Pathologic Findings		
P.B.	57	M	Pyriform sinus, floor of mouth palatine border	T_4N_0	Differentiated squamous cell carcinoma	6,000/68	300/150	No post-treatment surgery	None	Leukopenia 4,500 to 1,500 Day 18; 1,150 Day 81; 2,000 Day 112; anemia: hemoglobin 14.2 to 8.8 gm. per cent Day 81; recovery to 10.2 gm. per cent on Day 104	100 per cent tumor regression—5 months
S.Y.	72	F	Nose, nasal fossa	T_4N_0	Differentiated squamous cell carcinoma	7,250/54	108/81	None	None	Leukopenia 2,800 Day 42; spontaneous recovery	100 per cent regression of nasal fossa mass—6 months
A.D.	79	F	Parotid (recurrent)	T_1N_3	Adenocarcinoma	2,000/10	20/15	None	None	Leukopenia 5,250 to 1,000 Day 15; drug discontinued	100 per cent regression of 4 cm. neck mass
C.S.	46	F	Tonsil	T_2N_2	Anaplastic undifferentiated carcinoma	6,000/100	136/102	None	None	Severe nausea and vomiting; leukopenia 6,700 to 2,350 Day 36; spontaneous recovery	100 per cent regression-6 months; perigastric metastases
E.K.	51	M	Floor of mouth, base of tongue	T_4N_0	Undifferentiated squamous cell carcinoma	6,000/46	142/81	Composite with mandibulectomy and bilateral neck dissection	Invasive well differentiated squamous cell carcinoma floor of mouth; 28 lymph nodes negative; adequate margins	None	Tumor present in primary site
F.S.	64	M	Vallecula, epiglottis, vestibule	T_2N_0	Poorly differentiated squamous cell carcinoma	6,500/45	300/88	Multiple biopsies and radical neck dissection	Negative biopsies from hypopharynx; 16 lymph nodes negative	None	100 per cent tumor free at surgery and 3 months
E.S.	52	F	Tonsil, base of tongue	T_4N_2	Poorly differentiated squamous cell carcinoma	6,000/46	150/87	Excision of tonsillar fossa with radical neck dissection	Primary site no malignancy; 23 lymph nodes negative	Leukopenia 2,500 Day 15; 2,000 Day 36; spontaneous recovery Day 45. Anemia; hemoglobin 14.5 to 8.5 gm. per cent on Day 72	100 per cent tumor free at time of surgery and 5 months
S.S.	59	F	Tongue, lateral floor of mouth	T_2N_2	Moderately differentiated squamous cell carcinoma	4,200/37	52/39	Composite with hemiglossectomy and radical neck dissection	Ulceration of tongue with giant cells—no tumor; 20 lymph nodes negative	None	100 per cent presurgical eradication of tumor
G.S.	52	M	Larynx (supraglottic), hypopharynx	T_3N_0	Moderately well differentiated squamous cell carcinoma	5,500/53	280/206	Tracheostomy and rebiopsy (multiple)	Radiation effect—no tumor	Severe edema	100 per cent tumor free—6 months
B.M.	48	F	Palate (bilateral)	T_4N_3	Squamous cell carcinoma	6,000/68	84/126	None	None	Nausea and vomiting; leukopenia 2,100 Day 18; recovery Day 33. Anemia: hemoglobin 15.8 to 7.1 gm. per cent Day 69; transfusion; hemoglobin 11.6 to 8.6 gm. per cent Day 111	80 per cent regression—7 months; severe necrosis

TABLE III

RESULTS OF TREATMENT IN CONTROLLED STUDY

Modality of Treatment	No.	Tumor Regression (per cent)						
		100	75	50	25	0	M	D
Irradiation Alone	7	1	3	1	1	1	1	2
Irradiation+Surgery	13	13					2	1
Irradiation+Hydroxyurea	9	7	2					2
Irradiation+Hydroxyurea+Surgery	11	11						

Patients who had had no postirradiation surgery are summarized in Table III.

Group III consisted of 45 patients who were excluded from the controlled series by virtue of the fact that they had either received previous surgery or irradiation and had persistent or recurrent tumor. These patients received intermittent Hydroxyurea and irradiation. These patients are summarized as to response in Table IV.

COMPLICATIONS

1. *Gastrointestinal symptoms.* In patients receiving placebo, 2 of 20 patients experienced anorexia, nausea and vomiting. Of 60 patients receiving Hydroxyurea, 33 complained of anorexia, nausea and vomiting. In only 2 patients was it necessary to discontinue Hydroxyurea because of the vomiting. The suggestion by Squibb researchers that the large amounts of gelatin consumed with the capsules might be a factor was not substantiated by a decrease in symptoms when the gelatin powder was removed from the capsules.

2. *Hematopoietic depression.* (a) Leukopenia. Thirty-six of the 65 patients treated with Hydroxyurea developed leukopenia. This occurred between 11 and 36 days. Discontinuance of the drug resulted in a return to normal in 6 days. Frequently, a spontaneous return to normal occurred in a slightly longer period of time. In no patient did a leukopenia cause permanent cessation of drug therapy. Several patients exhibited recurrent leukopenia with recovery during

TABLE IV

SUMMARY OF RESPONSE TO CONCOMITANT USE OF HYDROXYUREA AND IRRADIATION IN PATIENTS WITH RECURRENT OR PERSISTENT NEOPLASIA

Site	Previous Treatment			Degree of Response (per cent)						
	Surgery	Irradiation	Surgery and Irradiation	100	75	50	25	0	M	D
Tongue	1		4	2	2		1			2
Parotid	6		1	6		1				
Tonsil	4			1	1	2				1
Hypopharynx	3			1	2					1
Larnyx	4	2	5	5	4	2				1
Nasopharynx	2			1		1				
Antrum	1				1					
Palate	1			1						
Nose	2			2				1		1
Esophagus	1									
Trachea	2			2						
Lip	1			1						
Buccal mucosa	1	2		1			2			2
Pulmonary metastasis			2	1	1					1

their prolonged period of therapy. A leukopenia due to irradiation was reported in 1 of 20 placebo patients. (b) Anemia. Twenty per cent (12/65) of the patients receiving Hydroxyurea developed an anemia in an average of 39 days. These responded to oral or intramuscularly injected iron salts. Five patients required transfusions. Megaloblastic changes were noted in both the peripheral blood and bone marrow in 3 cases. This has been previously reported by Thurman and Watkins.[10] (c) Thrombocytopenia. In no case did the platelet count fall below the critical level established at 100,000.

3. *Skin reactions.* Three patients developed a rash coincident with the administration of Hydroxyurea. In 1, the rash was papillary and in 2, macular. In all 3, it disappeared in 3–4 days following the discontinuance of the chemical, only to recur upon its re-institution.

Six patients complained of a cutaneous flushing sensation in the irradiated site similar to the phenomenon frequently seen with actinomycin D therapy.

4. *Mucositis and pharyngitis.* There was no evidence of intensification of the usual radiation effect on the mucous membrane of the pharynx and larynx.

Three patients developed postoperative mucocutaneous fistulae. Two had received a rapid course of irradiation. The third consumed large quantities of alcohol during the course of his treatment. It was felt that Hydroxyurea played no part in this complication.

5. *Vascular thrombosis.* Six (10 per cent) patients died of vascular thrombosis during the course of Hydroxyurea therapy (5 myocardial infarction, 1 cerebral thrombosis). There were no vascular accidents in the placebo group. Abnormal proteins, coagulants and altered blood viscosity are common findings in patients with malignancy. There was no obvious correlation between Hydroxyurea ingestion and vascular thrombosis.

DISCUSSION

Hydroxyurea ($CH_4N_2O_2$) has both inhibitory and cytotoxic effects on cancer cells. Philips *et al.*[6] reported Hydroxyurea as a selective inhibitor of DNA synthesis. Sinclair[8,9] believed that the lethal action of the drug was selective for cells in DNA synthesis (S cells) only. When added to cell culture it killed all S cells and blocked all cells at the end of the G_1 stage. The facts that Hydroxyurea is lethal to cells in the S stage, that a synchronization of cells to a relatively radiosensitive stage (G_1) occurs, that inhibited G_1 cells appear to be more sensitive to irradiation in the presence of Hydroxyurea, and that irradiation is selectively damaging to other stages of the cycle suggested to many observers that a combination of Hydroxyurea and irradiation would be more effective than either agent alone.

Lerner *et al.*[5] reported a series of 4 patients receiving concomitant Hydroxyurea and radiotherapy in head and neck cancer.

In the controlled double blind study, while there was a notable difference in the eradication of tumor in the primary site in patients undergoing operation following preliminary treatment, (6/11 receiving Hydroxyurea and irradiation revealed no tumor; 2/12 in the placebo plus irradiation group), the principal observation was a striking difference in the effectiveness of lymph node eradication (Table v). In the group receiving Hydroxyurea with irradiation, all lymph nodes removed possessed no viable tumor. The pathologist noted an unusually extensive coagulation necrosis of lymph nodes previously involved with cancer. Of the group receiving the placebo and irradiation, 7/12 revealed viable cells in lymph nodes.

Two impressions are evident:

(1) Surgery is a necessary adjunct and contributes appreciably to the 100 per cent eradication of the tumor. In all 26 patients operated upon in both groups, adequate margins were obtained and all local and regional tumor was removed. Those receiving Hydroxyurea in addition to irradiation have had no recurrence in a 3 to 7 month follow-up period. Five patients died, 3 with metastases, who did not have all 3 modalities of treatment (Table III).

TABLE V

COMPARISON OF PATHOLOGIC FINDINGS IN PATIENTS OPERATED UPON FOLLOWING TREATMENT

	Primary Site			Lymph Nodes		
	Positive	Negative	Positive with Radiation Effect	Positive	Negative	Positive with Radiation Effect
Group I Irradiation+Placebo	6	2	4	6	5	1
Group II Irradiation+Hydrea	4	6	1	–	11	–

(2) The most notable contribution of Hydroxyurea is to increase the effectiveness of irradiation in the eradication of tumor in lymph nodes.

For many reasons, 7 patients in Group I and 9 patients in Group II had no subsequent surgery. Seven of 9 receiving Hydroxyurea noted 100 per cent tumor regression. Of the 7 receiving the placebo, only 1 noted a complete tumor regression.

In the treatment of failures to other methods of treatment (Table IV) with concomitant Hydroxyurea and irradiation, the results are less impressive. Twenty-four of 45 demonstrated a 100 per cent local regression. All patients treated showed a measurable response. The decreased degree of response in these patients is probably due to circulatory changes attendant with the previous treatment. Nevertheless, the ability to fractionate irradiation when used with Hydroxyurea provides a satisfactory method of retreating otherwise untreatable recurrences.

SUMMARY

Forty patients were treated in a double blind study utilizing Hydroxyurea. Those treated with Hydroxyurea, irradiation and surgery achieved complete eradication of tumor.

The most notable contribution of Hydroxyurea appeared to be the extensive necrosis, radiation effect, and destruction beyond any recognition of tumor in lymph nodes.

Forty-five cases, previous failures to other modalities, were retreated with Hydroxyurea and irradiation with local regression of tumor in all cases.

George J. Richards, Jr., M.D.
Department of Radiology
Greater Baltimore Medical Center
Baltimore, Maryland 21204

The authors gratefully acknowledge Dr. Gerald L. Beckloff, Associate Clinical Research Director, the Squibb Institute for Medical Research, for his encouragement and assistance, the Squibb Institute for Medical Research for generously supplying Hydrea for this project, Mrs. Grace M. Campbell, R.N., for technical assistance and Miss Lynne Carre for her help in the preparation of this report.

REFERENCES

1. BECKLOFF, G. L., and LERNER, H. J. Concomitant use of hydroxyurea and x-irradiation in treatment of head and neck cancer. *Internat. Cong. Chemotherapy*, 1967, *5*, 353–359.
2. BECKLOFF, G. L., LERNER, H. J., COLE, D. R., and KILGER, K. Hydroxyurea in bladder carcinoma. *Invest. Urol.*, 1966, *3*, 530–534.
3. LERNER, H. J., and BECKLOFF, G. L. Combined chemotherapy and radiotherapy: preliminary results of clinical trial of hydroxyurea and x-irradiation in treatment of epidermoid cancers of head and neck. *Am. Surgeon*, 1967, *33*, 165–170.
4. LERNER, H. J., and BECKLOFF, G. L. Hydroxyurea administered intermittently. *J.A.M.A.*, 1965, *192*, 1168–1170.
5. LERNER, H. J., BECKLOFF, G. L., LIPSHUTZ, H.,

Campbell, R., and Ritchie, D. Hydroxyurea in management of head and neck cancer. *Plast. & Reconstruct. Surg.*, 1967, *40*, 233–239.

6. Philips, F. S., Sternberg, S. S., Schwartz, H. S., Cronin, A. P., Sodergren, J. E., and Vidal, P. N. Hydroxyurea. I. Acute cell death in proliferating tissues in rats. *Cancer Res.*, 1967, *27*, 61–74.
7. Phillips, R. A., and Tolmach, L. J. Repair of potentially lethal damage in x-irradiated HeLa cells. *Radiation Res.*, 1966, *19*, 413–432.
8. Sinclair, W. K. Hydroxyurea: differential lethal effects on cultured mammalian cells during cell cycle. *Science*, 1965, *150*, 1729–1731.
9. Sinclair, W. K. Hydroxyurea: effects on Chinese hamster cells grown in culture. *Cancer Res.*, 1967, *27*, 297–308.
10. Thurman, W. G., and Watkins, W. L. Study of serum B 12 and folate in patients treated with hydroxyurea (NSC-32065). *Cancer Chemother. Rep.*, 1964, *40*, 23–25.

LONG TIME SURVIVALS OF PATIENTS WITH CANCER OF THE EYE AND SURROUNDING STRUCTURES TREATED WITH RADIATION THERAPY*

By CHARLES L. MARTIN, E.E., M.D., F.A.C.R.
DALLAS, TEXAS

DURING my 48 years devoted to the practice of radiology it has been my good fortune to be invited to appear as a guest speaker before many cancer seminars and other groups interested in the treatment of malignant diseases. More recently I have been surprised by the opposition expressed by some of the younger ophthalmologists to the use of radiation in the treatment of cancer in and about the eye. After much thought, this paper, containing complete follow-up studies of 10 such patients taken from our files, is being presented. To me the presentation of a small group of representative patients, together with photographs and all available data, is more valuable than a mass of statistics.

In the interest of brevity, cancers of the eyelid, which have been successfully treated with x rays since the turn of the century, will not be discussed as an entity. A résumé of the bibliography covering the early publications dealing with the treatment of skin cancer including the eyelids is included in an article entitled "Squamous Cell Carcinoma of the Skin"[1] presented before this Society in 1932.

X-RAY TECHNIQUE

In 1920, after finishing a radiologic residency at the Massachusetts General Hospital, I returned to Dallas to form a partnership with my father, James. M. Martin, and take over the rather modest radiologic department which he had established at Baylor Hospital. In Boston cancer of the skin, including the eyelid, was quite rare and my father's success obtained with low voltage x rays alone made it obvious that I had a great deal to learn. At that time the quantity of radiation used was measured in terms of minimum erythema doses, and other factors such as kilovolts, milliamperes, target-skin distance, filters, and port sizes were also noted. It soon became apparent that my father's good results, particularly those obtained with the old style gas tubes, depended for the most part on his experience and clinical judgment. Of course, the Coolidge tube was available when I came on the scene but the establishment of a generally accepted "roentgen" and the production of practical instruments capable of measuring the ionization produced in small air chambers did not occur until the late 1930s. With these chambers our x-ray machines were calibrated in terms of roentgens per minute delivered in air at the lower ends of our treatment cones. These measurements, which can be made quickly with a reasonable degree of accuracy, are still used in our clinic today and the doses reported in this paper are all set down in terms of roentgens measured in air. This basic accurate figure together with the kv., target-skin distance, port size, filters and exposure time make it possible for one to obtain approximately accurate depth doses from published tables expressed either in roentgens or rads. I prefer to set down the factors known to be accurate and let the reader take it from there.

Generally speaking only 2 x-ray techniques were used in treating cancer of the eye and its adjoining structures. The superficial lesions were treated with a low voltage machine operating at 85 kv. with a target-skin distance of 16 cm., a filter of 0.5 mm. of aluminum and leaded glass cones vary-

* Presented at the Fiftieth Annual Meeting of the American Radium Society, Miami Beach, Florida, April 7–11, 1968.

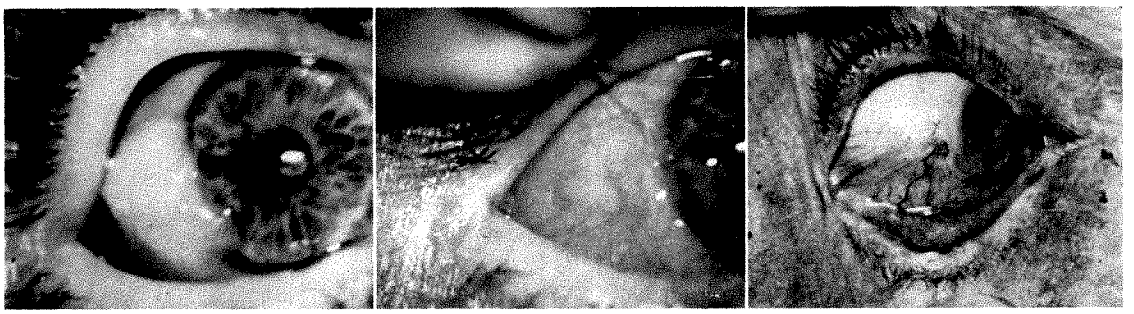


FIG. 1. Squamous cell carcinoma of the conjunctiva of the right eye overlapping lens margin before and 3 weeks after 6,000 r low voltage x-ray therapy. Photograph on right made after removal of a cataractous lens that appeared 17 years after treatment. Vision good with glasses and no evidence of cancer at 36 years.

ing from 2 to 4 cm. in diameter. A mild erythema was produced with 600 r and it was finally decided to treat small basal cell skin cancers with 4,800 r given in 4–5 days and squamous cell lesions with 6,000 r given in 5–6 days. A brisk reaction appeared in about 10 days but in most cases healing occurred in 6–8 weeks. The scars were smooth but some of them developed mild telangiectasia appearing 5 or more years after treatment. At the time of each treatment the cancer was placed in the center of a hole cut somewhat larger than the neoplasm in a thin sheet of lead foil. The foil removed from dental film packs is soft and possesses the correct thickness. Before it was placed in contact with the anesthetized conjunctiva it was first dipped in melted paraffin and then allowed to cool. When the eyelids were treated, a cup-shaped shield which incorporated a protective sheet of lead foil was first slipped under the anesthetized eyelids so that the cornea and most of the conjunctiva were completely protected. With small eyelid lesions a lead foil shield of the type described above was also used.

Deeper lesions were treated with orthovoltage machines operating at 200 to 260 kv. with a target-skin distance of 50 to 60 cm., filters with primary components of copper measuring 0.5 mm. or tin 0.4–0.8 mm. in thickness and portals varying from 2.5 cm. in diameter to 15×15 cm. square. The dosage measured in air will be described with each case. The importance of shielding the lens with lead strips measuring 2.0 mm. in thickness will also be discussed.

CANCER OF THE CONJUNCTIVA

In the beginning it was assumed that the conjunctiva of the exposed portion of the eye was very sensitive and could not withstand our dose of 6,000 r given in 5–6 days required for the actual cure of a squamous cell cancer of the skin. However, in 1930 it was discovered that when this dose was given to the relatively small lesions found growing on the conjunctiva the reaction was not severe and healing occurred with little or no scarring.

Our first patient with an adequate follow-up was admitted on December 28, 1931, with the large tumor shown in Figure 1 growing on the outer portion of the conjunctiva of the right eye. This lesion appeared after the second unsuccessful attempt at surgical excision. The biopsy examination was reported as low grade squamous cell carcinoma. This diagnosis was proven by a photomicrograph included in our previous article[1] published in 1932. A careful scrutiny of the first photograph indicates that the tumor overlapped the iris so that an opening in a treatment shield large enough to properly treat the tumor of necessity allowed irradiation of the outer edge of the lens. A dose of 6,000 r was given in 7 days using our low voltage machine. The tumor disappeared in about 3 weeks leaving very little scarring (middle

photograph). He did not lose the vision in the right eye until 1948 (17 years later) when the cataractous lens was removed. In 1962 the lens of the left eye, which was not irradiated, was also removed because of the presence of a senile cataract when he was 81 years of age. Now, 36 years after he was treated with radiation, he has 20/20 vision, with glasses, in both eyes and says that his eyesight is excellent. The photograph on the right side of Figure 1 shows the appearance of the right eye at the present time. The central defect is that usually observed after a cataract operation and no evidence of cancer can be seen.

Another patient with a large squamous cell carcinoma growing on the conjunctiva of the nasal side of the left eye and slightly overlapping the cornea was admitted on August 17, 1937. We decided to try to avoid cataract formation by giving only 2,400 r in 9 days, again using our low voltage equipment. The upper pair of photographs in Figure 2 show the tumor and its complete resolution in 2½ months. At first, the result obtained in this case indicated that the problem was solved but he returned 13 years after his first treatment with a recurrent carcinoma that had been growing in the original site for 3 years. At this visit the tumor received 6,000 r in 6 days and it has not recurred after 17 years. He now shows no evidence of cancer 30 years after his first visit but he developed a cataract in the left eye 7 years after his second treatment. The vision in his right eye is good and his ophthalmologist has elected not to remove the cataractous lens in the left eye. He is now 67 years of age.

The lower pair of photographs in Figure 2 show a smaller carcinoma of the conjunctiva in the outer right eye not involving the cornea before and 3 months after the administration of 6,000 r in 5 days to the tumor. The patient has now been well for 17 years and shows no evidence of cancer or cataract in the treated eye at the age of 62 years.

These cases indicate that even when only the edge of the lens is included in the field receiving a cancerocidal dose a cataract in the lens may occur often many years later. Of course, some might contend that these patients, especially the older ones, might develop such cataracts, even if no radiation therapy had been used.

This problem was thoroughly explored by Merriam and Focht[5] and their conclusions were reported in 1957. They studied patients treated with radium and radon seeds and others treated with orthovoltage and low voltage x rays. Some received single doses and in others the doses were fractionated up to 3 weeks and 3 months. Irrespective of the technique used it was shown that every lens receiving 1,150 r or more developed a cataract, while some of those receiving smaller doses did not.

CANCER OF THE INNER CANTHUS

This type of cancer usually begins in the skin of the lateral bridge of the nose and slowly extends downwards so as to invade the inner portions of both eyelids. Fortunately the lesion is almost always a basal cell epidermoid carcinoma. A typical case is illustrated in Figure 3. The patient was a woman 78 years of age, admitted on June 21, 1957, who had known that the tumor was present for 5 or 6 years but had received no treatment because she had no pain.

Here again it is necessary that the lens be protected. In early cases the eye is anesthetized with cocaine used in the form of drops and a cup-shaped device containing a thin lead shield is inserted beneath the eyelids so that it shields all of the cornea and the exposed portion of the globe. In the case shown in Figure 3 this procedure was impossible because the tumor filled so much of the aperture that the cup-shaped device could not be inserted. Instead the rounded end of a flat strip of lead measuring 1.0 mm. in thickness was inserted under the growing edge of the tumor and strapped over the normal portions of the eyelid so as to cover the cornea. The remainder of the tumor was sur-

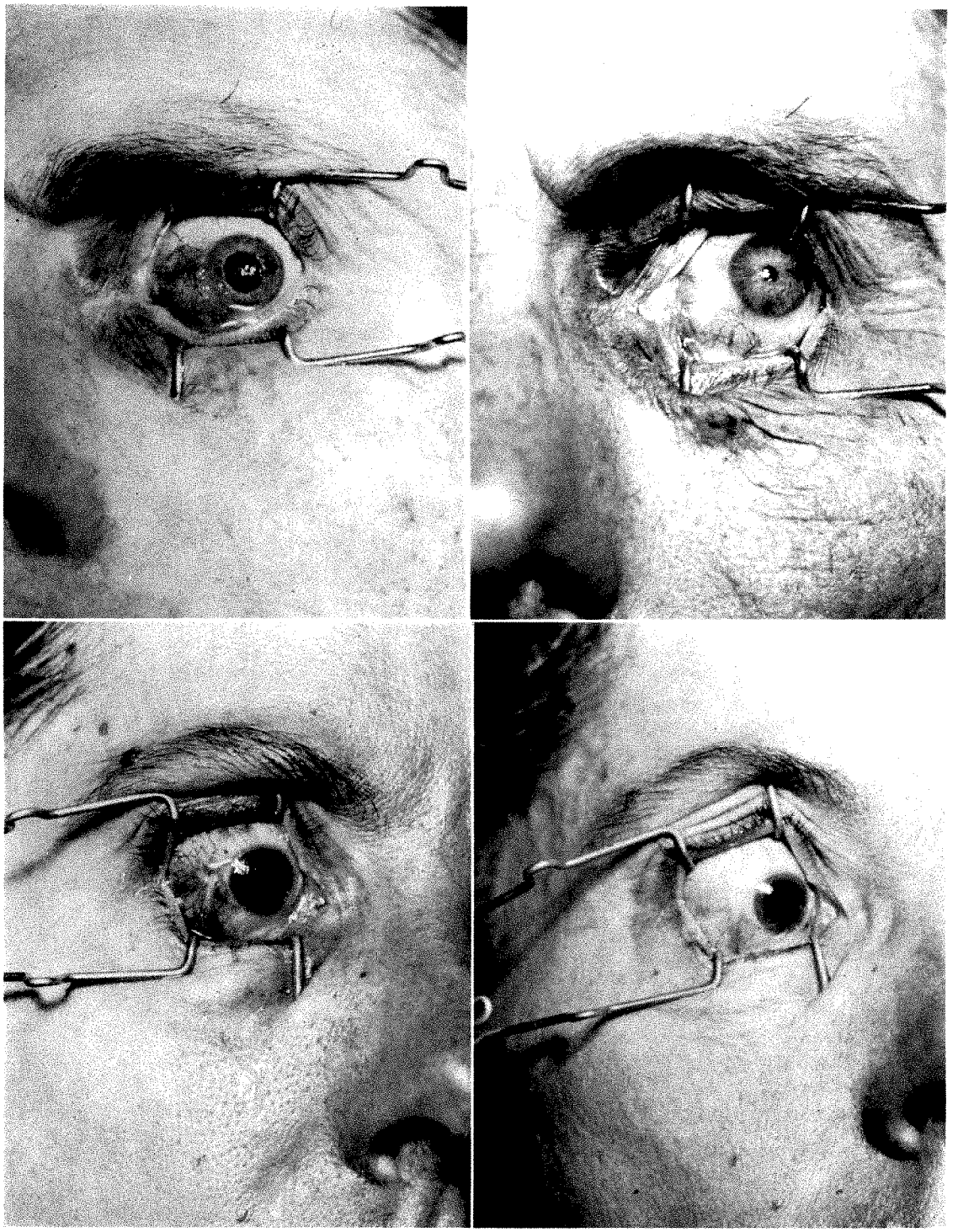


FIG. 2. *Upper Photographs.* Squamous cell carcinoma of conjunctiva of left eye overlapping lens margin before and 6 weeks after 2,400 r low voltage x-ray therapy. Cancer recurred at 10 years and received 6,000 r at 13 years. Cataract appeared 12 years later. Well with no cancer 30 years after first treatment.
Lower Photographs. Small squamous cell carcinoma of conjunctiva of right eye not overlapping lens before and 6 months after receiving 6,000 r low voltage x-ray therapy. Well 17 years with no cataract.

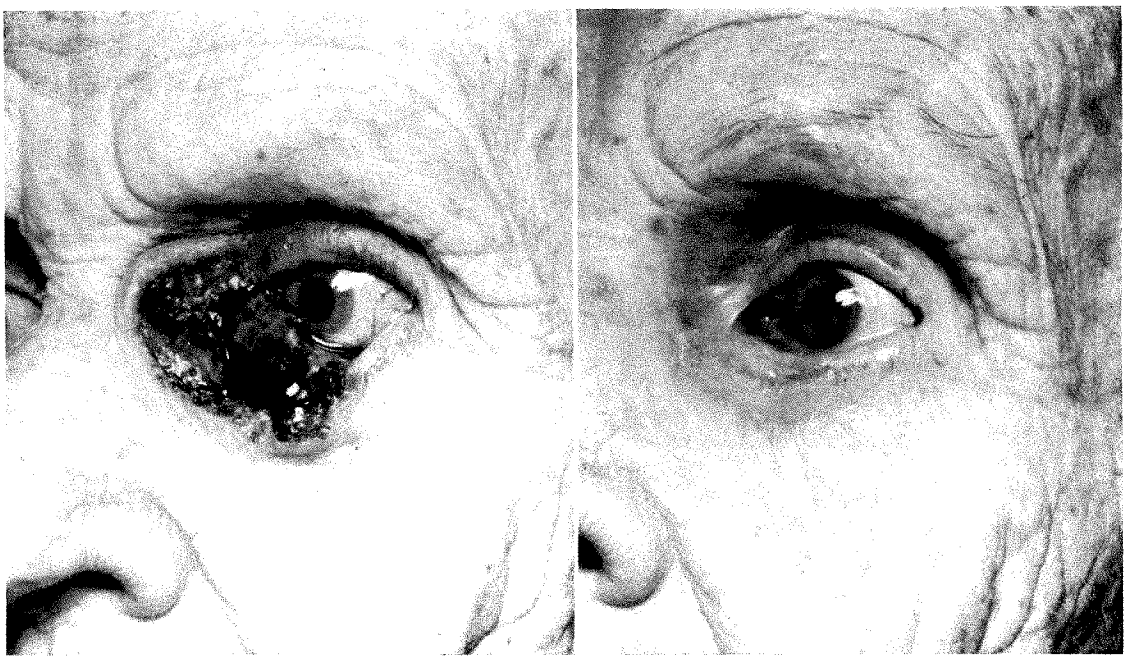


Fig. 3. Large basal cell carcinoma of left inner canthus before and 6 weeks after administration of 4,800 r low voltage x-ray therapy with complete shielding of left eye. Died 8 years later of heart failure with no evidence of a recurrence or cataract but complained of tearing.

rounded by the thin sheets of lead foil cut out to provide a portal somewhat larger than the neoplasm. A dose of 4 times 1,200 r was given during a period of 5 days through a leaded glass cone just large enough to cover the portal, using our low voltage technique. Everything used in and about the eye was sterilized in 70 per cent alcohol and then thoroughly rinsed with sterile saline solution. Since the anesthetic dilated the pupil such patients were warned that they must not drive a car until the effects of the anesthetic had worn off.

The photograph on the right side of Figure 3 made 6 weeks after treatment shows a complete disappearance of the neoplasm. The eyelashes in the treated area were gone but her only troublesome complaint was that of epiphora, produced by the occlusion of both tear ducts which were incorporated in the malignant tissue. Healing following successful radiation therapy of necessity produces fibrosis about the tiny ducts and we have discovered no method of preventing the obstruction produced in cured cases. This patient showed no evidence of a recurrence of cancer when she died of heart failure at the age of 85 years, 8 years after she received radiation therapy.

A more advanced basal cell cancer involving both inner canthi is shown in Figure 4. This patient was admitted on September 10, 1951, when she was 65 years old. The tumor originated on the bridge of the nose and grew laterally in both directions so as to involve the inner portions of both eyelids of both eyes. She was a Christian Scientist and could not be induced to seek treatment until the large tumor began to interfere with her vision. Oval shields cut from a sheet of lead 2.0 mm. thick were placed over both eyes and the portions of the tumor originating in the eyelids. A dose of 12×300 r was then given in 13 days to the very thick growth on the bridge of the nose through a portal measuring 8×10 cm., using orthovoltage equipment operated at 200 kv. with a filter of 0.5 mm. of copper and 1.0 mm. of aluminum and a target-skin



FIG. 4. Large basal cell carcinoma of bridge of nose with extension into the eyelids on both sides before and 6 months after 3,600 r given with orthovoltage therapy to central lesion and 4,800 r low voltage x-ray therapy given first to inner eyelids on one side and then the other with careful shielding of eyes. Died 2 years later following automobile accident with no recurrent cancer in face and no cataracts.

distance of 50 cm. Two months later when the central tumor showed much shrinkage, doses of 4 times 1,200 r, generated at 85 kv. with a filter of 0.5 mm. of aluminum and a target-skin distance of 16 cm. were given daily through lead glass cones, just large enough to encompass the residual tumor tissue in the inner eyelids, first on one side and then the other. Preceding each treatment our cup-shaped eye shields were slipped under the eyelids so as to completely shield the eyes. The photograph on the right side of Figure 4 was made 6 months after the first visit when there was no evidence of cancer made out. The vision in both eyes was normal and the small hole through the right side of the bridge of the nose, secondary to a malignant perforation, was healing. She was seriously injured in an automobile collision 2 years after her radiation therapy and was taken to a hospital where a fractured hip was discovered. Soon afterward she died with symptoms suggesting pulmonary fat embolism. No evidence of her original cancer was observed at the time of death.

Perhaps the most distressing problem confronting head and neck surgeons and radiotherapists alike is shown in Figure 5. When this 36 year old woman was admitted on October 28, 1940, she stated that a cancer limited to the skin of the bridge of her nose had been treated unsuccessfully in a small town 5 years previously. She did not realize the seriousness of her trouble until the tumor extended into the left orbit and caused a great deal of pain. She then again consulted her physician who sent her to our clinic with the appearance illustrated in the photograph on the left side of Figure 5. It is obvious that following the production of a large mass in the left inner canthus similar to the one shown in Figure 3, the neoplasm grew steadily to fill the left orbit



FIG. 5. Mixed basal and squamous cell carcinoma of the skin of the bridge and left side of nose with deep extension into the left orbit, nasal cavity and antrum before and 1 year after 3,600 r (orthovoltage) given through a 10×10 cm. port. With palliative x-ray therapy and surgery at long intervals she looks well, with a new recurrence, at 27 years after her first visit.

and destroy the eye. The nasal wall and floor of the orbit were also destroyed and tumor tissue was detected in the nasal passage and the left antrum. The original skin lesion had also extended downwards along the left wall of the nose to involve the nasolabial fold. A biopsy specimen was reported as a mixed basal and squamous cell carcinoma.

In the 1930s many such cases came to us after radical surgery had destroyed most of the face and we were able to provide little more than temporary improvement because of the extensive bone invasion. Fortunately the patient shown in Figure 5 had only moderate bone involvement and we decided to try orthovoltage therapy first, with the thought that secondary surgery would not produce marked disfigurement. An oval lead shield measuring 2.0 mm. in thickness was fixed between 2 ovals of leaded rubber cut from an old fluoroscopic apron and strapped over the right eye. Twelve doses of 300 r were then directed vertically at a portal measuring 10 ×10 cm. arranged to cover the nose, left orbit and left cheek in a period of 13 days. The treatment factors were 220 kv., a Thoraeus filter with a primary element of 0.8 mm. of tin and a target-skin distance of 50 cm. The skin reaction was severe and as the tumor tissue melted away the remnant of the left eye became apparent and was removed by her home physician a little later. All of her pain disappeared and she began to gain weight and felt well again. The photograph on the right side of Figure 5 shows her appearance at the end of 1

year. Small fistulae communicated with the orbit and antrum and produced small amounts of drainage.

She returned to our clinic at the end of 14 years with small recurrences in the original areas observed at her first admission. She again received 12×300 r in 13 days but the treatment was given through a round portal measuring 7 cm. in diameter. At 13 years she returned with necrotic tissue in the edges of an ulcer on the left side of the nose. This tissue together with the underlying dead bone were removed by a good cancer surgeon and a graft was placed over the defect.

She felt well until September 6, 1958, when she came in with a cauliflower tumor measuring 2×3 cm. growing on the left side of the bridge of the nose. Since she had not been treated for 4 years this smaller tumor was again given 12×300 r with the technique used at the previous visits.

She felt well until October 6, 1967 (27 years after her first visit) when she returned with frontal headache and recurrent cancer in the edge of a wound which opened into the left orbit and antrum. The exposed bone was definitely necrotic. At this visit we destroyed the visible malignant tissue with electro-surgery, and removed most of the dead bone with rongeur forceps. She still looked well. Our palliative treatment will be condemned by most surgeons but radical surgical procedures would have left her without a nose and most of the left face and she would probably have had a ghastly appearance with residual tumor still located deep in the bony structures of the face.

Extension of cancer into the orbit does not always originate in the skin of the nose but may extend upwards from a cancer of the cheek as illustrated in Figure 6. This 71 year old woman was admitted on June 12, 1950, with a very large nodular squamous cell carcinoma, Grade III, of the entire right cheek which had destroyed the right malar bone by pressure and extended over the lower rim of the orbit so as to extend behind the globe of the right eye. No metastases could be discovered in the cervical lymph nodes or the mandible or skull. The central portion of the tumor measured about 2.5 cm. in thickness and many nodules and areas of ulceration were seen on its outer surface. A capable physician observed this growth when it measured about 1.0 cm. in diameter and was located in the skin of the mid portion of the right cheek, 2 years before admission. His insistence that it receive immediate treatment was ignored bacause of the absence of pain.

After some deliberation it was decided that no attempt be made to save the right eye and 12 × 300 r were given in 13 days through a 15×15 cm. port large enough to include the right eye, but the right ear and left eye were shielded. The other factors were 200 kv., a filter of 0.5 mm. of copper and 1.0 mm. of aluminum and a target-skin distance of 50 cm.

The reaction was rather severe but at 6 weeks the nodules were gone and the skin in the central area was denuded. At 3 months (upper right photograph, Fig. 6) the denuded area was closing in. At 1 year the denuded area had almost completely healed but a painful conjunctivitis was developing in the right eye. Enucleation of the eye was advised but was not carried out until 2 years after the radiation therapy. At that time the denuded area on the right cheek had healed. The photograph in the lower right portion of Figure 6 made 8 years after treatment shows a smoothly healed scar on the right cheek. The depression in its central portion resulted from the absence of the right malar bone which is well shown in the adjoining roentgenogram. Her physician reported that she had no recurrence in the right cheek or orbit when she died at the age of 80 of heart failure, 9 years after she received radiotherapy.

Not all of the neoplasms growing in the orbit arise from outside sources. A 5 year old boy was admitted on October 26, 1946, after a biopsy had proved a nodular tumor felt behind a ptosed left upper eyelid to be a rhabdomyosarcoma. At that time results



FIG. 6. Large squamous cell carcinoma of the entire right cheek with extension deep into the right orbit before and 1¼ years after the delivery of 3,600 r (orthovoltage) to a 15×15 cm. port laid out to include the right eye. The damaged eye was enucleated at 2 years. The pressure destruction of the right malar bone shown in the roentgenogram explains the deep crease in the healed scar. When she died of heart disease 9 years after treatment, no evidence of cancer of the cheek could be found by her physician.



FIG. 7. Photographs show a 5 year old boy with low intensity radium needles implanted through a ptosed upper lid into a rhabdomyosarcoma of the upper left orbit and his appearance 11 years and 5 months later (middle photograph) when the left eye was rotated upward and his vision was impaired because of cataractous changes in the upper portion of the lens. At 21 years (right photograph) he is free of tumor and leads a fairly normal life, with the position of the left globe improved.

obtained after exenteration were rather poor and we were asked to try a low intensity radium needle implantation.[2] Four 1.33 mg. radium needles were inserted through the upper lid in a fan shaped pattern in a horizontal layer in the center of the tumor, and 2 small 0.66 mg. needles were placed transversely between the outer ends of each outer pair of the longer needles, after which they were all stitched in place for 7 days. The photograph on the left side of Figure 7 indicates that the young patient was not inconvenienced by the implanted needles during his hospital stay.

At 6 weeks all evidence of the tumor was gone but the left eye appeared to be rotated upward.

The middle photograph in Figure 7, made 11 years and 5 months after his radium implantation, showed the same upward rotation of the left eye apparently produced by a fibrosis in the left superior rectus muscle from which the rhabdomyosarcoma had probably originated. The boy was in excellent physical condition and was going to high school where he played in a marching band. His ophthalmologist reported that the vision in the left eye was somewhat impaired.

Soon after this check-up we lost contact with him and his parents. Since I felt that he might be one of our first patients cured with radiation alone, I instituted a search enlisting the help of friendly physicians in 2 states and finally received a letter from him on October 19, 1967, stating that as a member of the Mormon church he was expecting to serve a mission which would take him first to Louisville, Kentucky. A letter to the Chief of Radiology in the medical school there brought about an examination by the Professor of Ophthalmology which was quite thorough. His report with many photographs indicated that this patient, treated only with implanted low intensity radium sources, was free of any evidence of rhabdomyosarcoma 21 years after treatment. The vision in the left eye was impaired (20/50+2) and a cataractous change was seen in the left upper lens but he was able to carry on a normal life doing such things as reading music, typing and driving in a satisfactory manner. One of his photographs (right side of Fig. 7) also indicated that the position of the globe of the left eye was much better than it had been at his previous visit. This improvement may have resulted from two attempts made by his home ophthalmologist in 1958 to stretch the superior rectus muscle on the treated side.

Most ophthalmologists do not favor radiation therapy for the treatment of rhabdomyosarcoma. Porterfield and Zimmerman[6] reported in 1962 that not 1 of 55 cases treated with radiation was alive for 3 or more years and Reese[7] in the second edition of his book on tumors of the eye says that "some of these tumors appear to be somewhat radiosensitive but it is my feeling that x-ray therapy cannot be relied on as a curative measure."

However, Sagerman[8] and his associates at the Columbia-Presbyterian Medical

Center in New York have recently reported 5 cases well from 16 to 53 months after the administration of 5,000 rads directed through the eye to include the entire orbit and other invaded tissues in periods of 20–23 days. The equipment used was a 22.5 mev. betatron or a cobalt 60 teletherapy unit. Small posterior lens cataracts were observed in the cases followed 42 and 53 months and it seems likely that they will appear in the other cases in time.

A cursory search of the literature has turned up no case treated with implanted low intensity radium needles and it is just possible that this method which limits the cancerocidal dose of gamma rays to the tumor while delivering much smaller doses to the adjoining normal tissues may be of great value, particularly in the treatment of early cases.

CANCER OF THE GLOBE

We became interested in retinoblastoma in 1936 after reading a preliminary report published by Martin and Reese[3] indicating that this neoplasm might be controlled with x-ray therapy. Their next article[4] published in 1942 described the technique devised by Hayes Martin and their encouraging results.

Our first case, a baby boy 13 months of age, was admitted on April 15, 1946 soon after the enucleation of the globe of the left eye which was filled with a tumor diagnosed as retinoblastoma. An examination of the right eye revealed a detached retina that made it impossible for the ophthalmologist to visualize a secondary retinoblastoma which he felt certain was present. Doses of 400 r were given alternately to round ports measuring 1 inch in diameter located in the right temple and the nasal side of the left orbit and directed at the posterior portion of the globe of the right eye until 8,000 r had been given to each port in a period of 40 days. During each treatment one of three members of the family held the head of this very strong and active baby in its proper position against the treatment cone after his body had been tightly strapped to the treatment table. At 4 months the vision in the right eye slowly disappeared with the formation of a cataract. The ophthalmologist who could no longer see into the right eye enucleated it because he thought there was still some tumor present. However, a careful examination done by a good pathologist revealed no evidence of retinoblastoma. The bridge of the nose slowly disappeared making the boy's face unsightly.

He grew into a strong well developed man who was very bright and graduated from a school for the blind unusually well informed.

He was quite well 20 years after his treatment but near the end of his 20th year an undifferentiated epidermoid carcinoma appeared in the nose and rapidly invaded the left lateral pharynx and cervical lymph nodes. These lesions disappeared following low intensity radium needle implants and moderate doses of x rays over the neck but severe pain in many of his bones responding temporarily to moderate doses of x rays appeared and bone marrow biopsies indicated that the marrow was being rapidly invaded. No treatment available to us was effective and he died near the end of his 20th year following treatment.

Many who have studied this case record feel that the very intensive x-ray therapy may have induced the growth of the new neoplasm 20 years after treatment.

Our second case was another boy, 16 months of age, admitted on April 6, 1949, after the enucleation of the left eye and part of the optic nerve because of the presence of a retinoblastoma filling most of the globe. He was sent to our clinic following the discovery of a tumor in the upper nasal portion of the globe of the right eye. The x-ray technique was the same as that used in the first case except that we made an attempt to give more protection to the lens and the bridge of the nose. The treatment factors in both cases were 200 kv., a filter of 0.5 mm. of copper and 1.0 mm. of aluminum and a target-skin distance of 60 cm. No attempt was made to estimate the tumor dose which was much larger than those used by us in treating neoplasms in other parts of the body. The skin reactions

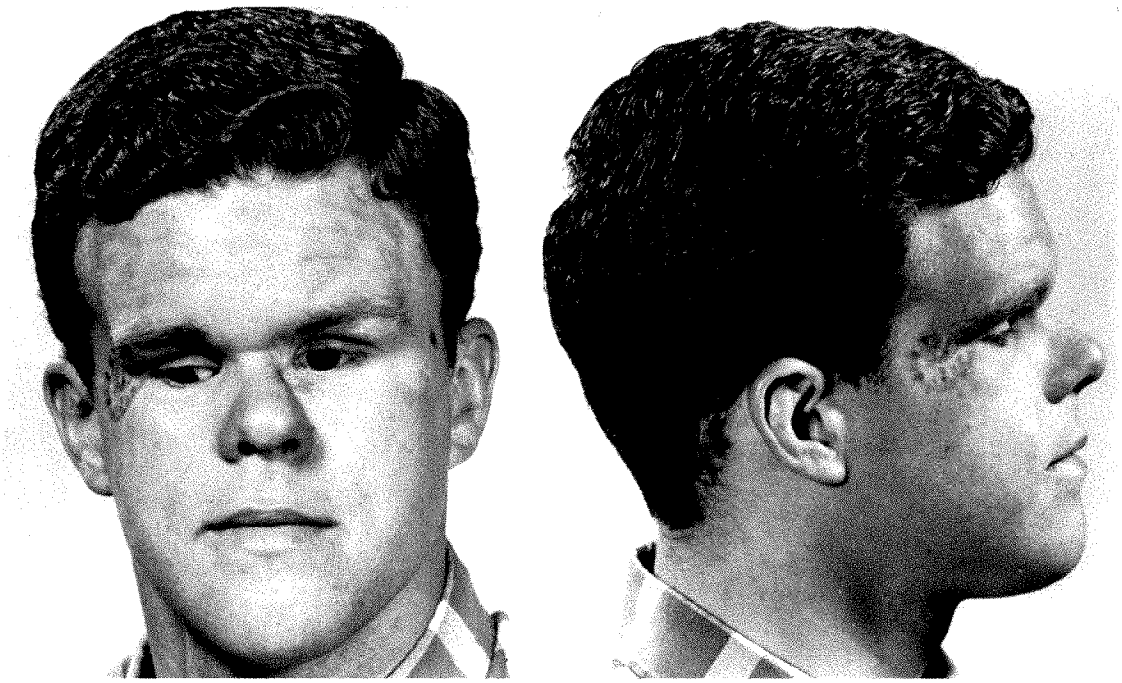


FIG. 8. Photograph of a young man 18 years after the enucleation of the left eye for retinoblastoma and the delivery of 8,000 r (orthovoltage) to each of 2 round, 1 inch ports directed at a secondary tumor in the nasal side of the globe of the right eye. The vision in the treated eye disappeared 4 years after treatment but the retinoblastoma was cured and he is now well developed both mentally and physically although totally blind.

were severe but finally healed with much scarring. The vision in the treated eye was good for 4 years after which it began to worsen and he became totally blind in the 5th year.

He now looks and feels well 18 years after his radiation therapy (Fig. 8). He wears a false eye on the left side but the right eye is still in place although totally blind and the deformity of the bridge of the nose is hardly noticeable. He is unusually well developed both physically and mentally and after graduation from a school for the blind has just entered the University of Texas. He swims, practices judo, at which he is said to be good, and is attempting to acquire a good education.

In his latest text book Reese[7] states that from 1936 to 1952 a total of 203 patients received the very intensive treatment described above with an estimated tumor dose of 10,800 r. The over-all cure rate with vision was 36 per cent but 12 per cent had very limited vision.

Because of the undesirable sequelae, he has in recent years been reducing the dosage and using various types of radiation augmented by chemotherapy, light coagulation, diathermy and the laser beam in an effort to better his end results. In 1963 he was giving most of his patients a tumor dose of 3,500 r generated by a 22.5 mev. betatron augmented by doses of T.E.M. Although his results were promising the number of patients treated and the follow-up times were then inadequate.

CONCLUSION

Complete follow-up records of 10 patients with malignant tumors in and about the eye treated with the older time tried radiologic techniques from 1931 to 1951 are described in some detail for the benefit of the younger radiotherapists and particularly for the benefit of the younger ophthalmologists, many of whom seem to view such procedures as dangerous and of little value.

The neoplasms treated were:

1. Superficial lesions including those

arising from the eyelids, inner canthus and conjuctiva.

2. Orbital lesions including invasions from cancer of the skin of the nose and cheek and a primary rhabdomyosarcoma.
3. Tumors in the globe of the second eye following enucleation of the first eye for retinoblastoma.

4605 Watanga Road
Dallas, Texas 75209

REFERENCES

1. MARTIN, C. L. Squamous cell carcinoma of skin. AM. J. ROENTGENOL. & RAD. THERAPY, 1932, *28*, 728–737.
2. MARTIN, C. L. Low intensity radium element needles. Janeway Lecture, 1949. AM. J. ROENTGENOL. & RAD. THERAPY, 1949, *62*, 467–492.
3. MARTIN, H. E., and REESE, A. B. Treatment of retinal gliomas by fractionated or divided dose principal or roentgen radiation: preliminary report. *Arch. Ophth.*, 1936, *16*, 733–761.
4. MARTIN, H. E., and REESE, A. B. Treatment of retinoblastoma (retinal glioma) surgically and by irradiation. *Arch. Ophth.*, 1942, *27*, 40–72.
5. MERRIAM, G. R., JR., and FOCHT, E. F. Clinical study of radiation cataracts and relationship to dose. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1957, *77*, 759–785.
6. PORTERFIELD, J. F., and ZIMMERMAN, L. E. Rhabdomyosarcoma of orbit: clinicopathologic study of 55 cases. *Virchows Arch. path. Anat.*, 1962, *335*, 329–344.
7. REESE, A. B. Tumors of the Eye. Second edition. Harper and Rowe, New York, 1963.
8. SAGERMAN, R. H. Personal communication.

VOL. 105, NO. 3

AN EVALUATION OF THE MANCHESTER SYSTEM OF TREATMENT OF CARCINOMA OF THE CERVIX*

By GEORGE SCHWARZ, M.D.†
BRONX, NEW YORK

THE Manchester system of treatment of carcinoma of the cervix was originally described by Tod and Meredith in 1938[23] and slightly altered in 1953.[24] The delivery of predetermined doses to fixed points related to the radium sources is the keystone of the system. Intracavitary radium alone is used in Stages I and II; in Stage III disease, 3,000 rads of parametrial irradiation (10 cm. high portals) is added.[17,18] The dosage at a point in the paracervical triangle (Point A) was chosen to permit a correlation of dose and clinical effect and to provide a maximum number of cures with a minimum number of complications when an optimal dose was delivered thereto. The dose at Point B represents the dose to the pelvic wall lymph nodes.

The purpose of this report is to present the relationship of this system to actual anatomy and patterns of cancer growth, and to examine its results.

DEFINITION OF POINTS A AND B

Point A was originally defined[23] in a frontal plane, 2 cm. lateral to the uterine canal, and 2 cm. up from the lateral fornix. In 1953 Tod and Meredith[24] redefined its location as 2 cm. from the end of the lowest uterine source (level of internal os), then 2 cm. laterally in the frontal plane. The loading of the tandem and ovoids was also slightly altered in 1953.[24] With colpostats which are located in the fornices with the cervix in between, Batley and Constable[2] advise the use of the original definition of Point A. Paterson[16] determined the optimum dose at Point A to be 8,000 r delivered in 2 insertions of 3 days each, separated by a period of 4 to 7 days. Actually, the treatment was determined by time of application, to quote, "For this technique—radium three days, rest four or seven days, radium three days—8,000 r seems optimum."

An ideal normal cervical and paracervical anatomy is not present in many clinical situations, either because of disease, obstetrical trauma or old age. Shortening of the fornices following obstetrical trauma produces an inferior displacement of the involved fornix. Many elderly patients have a narrow nondistensible vault, the fornices are entirely absent, and the location of Point A cannot be determined according to the original definition. Parametrial invasion in Stages II and III will also result in Point A being surrounded by tumor. Displacement of the cervical os to a corner of the vaginal vault, lateral displacement of the uterus by unilateral disease, a large fungating mass filling the upper vault of the vagina, or invasion of the isthmus (producing the so-called barrel-shaped cervix) are frequently encountered situations. Point A in these anatomic situations is not in the paracervical triangle and the dose at this point is not a reliable indicator of minimum tumor dose. Often also the dose at right Point A is not the same as left Point A (Fig. 1, *A–F*).

Adequate dosage to the periphery of the tumor during the first insertion is present only in small lesions, and the two closely-spaced radium insertions do not allow time for interval shrinkage of the tumor bulk nor for significant improvement of the radium geometry by the time of the second insertion. In the presence of bulky Stage I and II disease, when the tumor extends laterally and superiorly to Point A, it is difficult to understand the significance of de-

* From the Division of Radiotherapy, Montefiore Hospital and Medical Center and the Albert Einstein College of Medicine, Bronx, New York.
† Assistant Professor of Radiology, Albert Einstein College of Medicine.

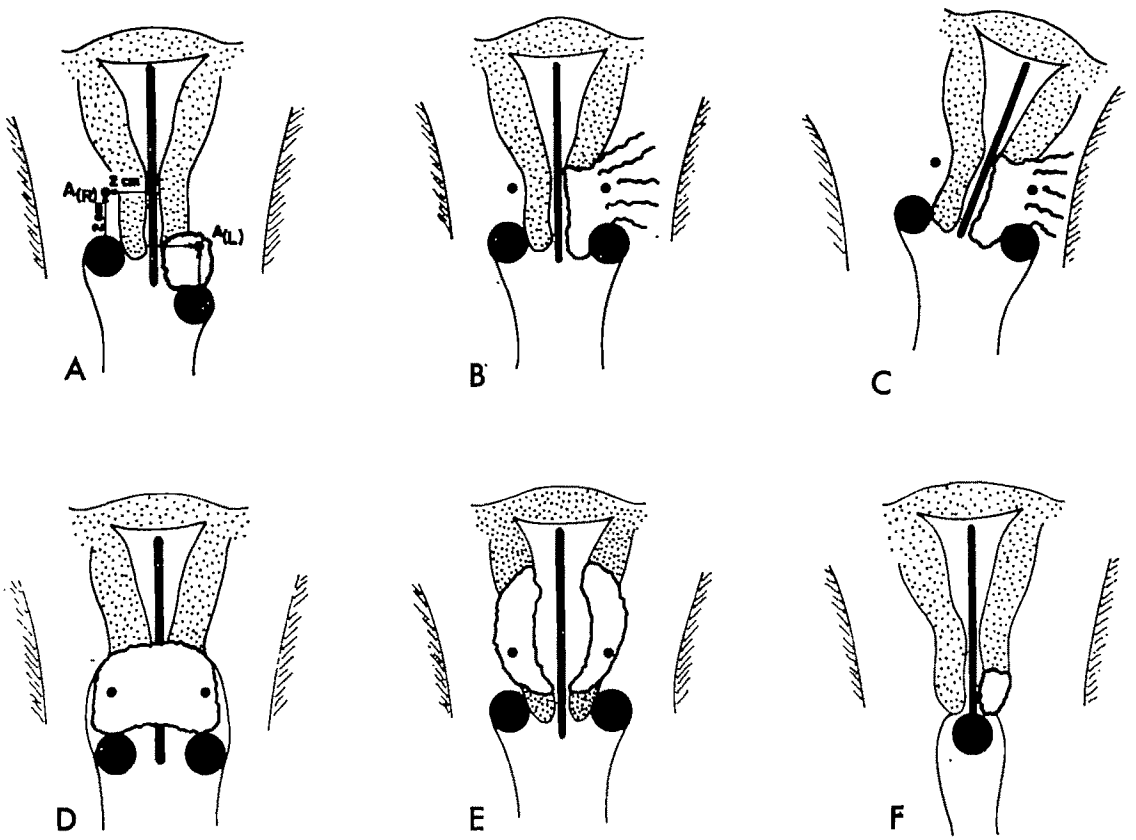


Fig. 1. (*A*) Point A is displaced downward on the left and lies in midst of tumor growing into the fornix. Dose rate at Point A on the left is lower than on the right. (*B*) The significance of dose rate at Point A on the side, in the center of tumor in the parametrium, bears little relationship to that of its counterpart on the right. (*C*) Parametrial shrinkage, in this case secondary to parametrial invasion, can produce anatomic asymmetry and a distinct difference of Point A on each side. Here, dose will be markedly higher on the left. (*D*) A large exophytic mass does not allow insertion of the vaginal applicators into the fornices, thus placing Point A in the middle of bulky neoplasm. (*E*) In this barrel-shaped cervix, enlarged by massive tumor, both Points A are buried within the depth of the lesion. (*F*) A narrow vault with or without encircling disease is often encountered in elderly patients. In the absence of fornices the position of Point A cannot be fixed.

livering a specified dose to that point. The dose of importance is the one delivered to the periphery of the tumor and, of course, no indication thereof is given by Point A.

Point B is defined as lying 3 cm. lateral to Point A. Figure 2 demonstrates that the regional lymphatics are, with the exception of the obturator lymph nodes, outside of the true pelvis. The traced area shows the range of location of Point B; in a young woman with a distensible vagina, Point B is at the obturator lymph node; if the vagina is short because of disease or old age, Point B lies below the lymph nodes.

Results of Treatment with the Manchester System

Since the value of any technique has to be ultimately judged on its results, the results obtained at Christie Hospital by the exclusive use of the Manchester system should be compared with those obtained at other institutions using different techniques. Table 1 lists the 5 year apparent recovery rates following treatment for carcinoma of the cervix in 5 centers.[1,3,15]

The radiation techniques used at the 4 institutions reporting higher survival rates than Christie Hospital will be briefly de-

scribed. The approach used by Kottmeier at the Radiumhemmet in Stockholm[12,13] is characterized by fractionated, high intensity intracavitary radium therapy. The insertion time for each application is about 24 hours, with at least a 2 week interval between insertions. Radium distribution varies greatly and is individually tailored to the pattern of growth. For instance, an endocervical lesion with barrel-shaped expansion is primarily treated with intrauterine and endocervical radium sources, whereas an exophytic lesion on the portio is treated by intrauterine radium and vaginal radium in equal proportions. External irradiation is added in all stages following radium therapy, but in bulky lesions it becomes the initial form of treatment.

At the M. D. Anderson Hospital in Houston,[10] whole pelvis irradiation is used as the initial form of treatment except in lesions which have little bulk (less than 3 cm. in diameter) and a local anatomy suited for effective radium applications, *i.e.*, room for at least two intrauterine sources and a width of vault adequate for at least small ovoids. The radium insertions are 2 weeks apart, they number more than 2 if further shrinkage is required or anatomic distortion makes impossible the simultaneous application of tandem and colpostats. The technique at the University of Maryland Hospital[3] is very similar to that used at the M. D. Anderson Hospital. At the Puerto Rico Nuclear Center[15] all stages of carcinoma of the cervix are first treated with external irradiation to a dose of 4,500 rads given 3 times weekly in 6 weeks, to be followed later by intracavitary radium therapy.

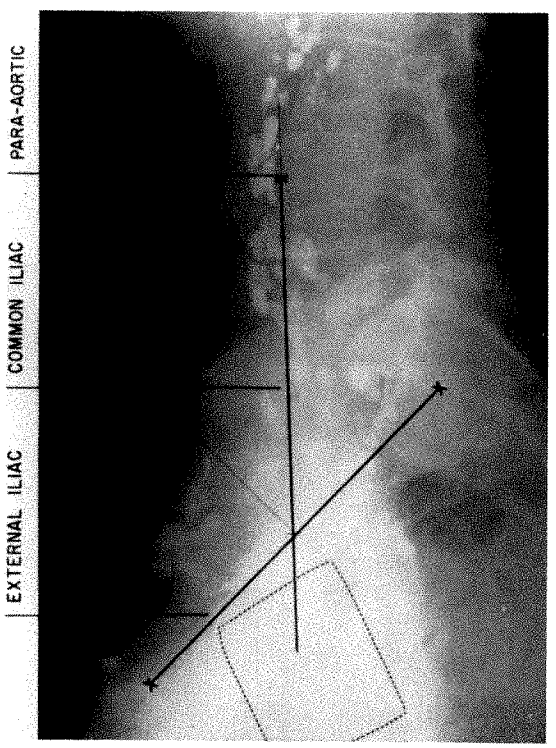


FIG. 2. The area with the rectangle is the range of location of Point B. With a distensible vault it is in the upper part, in the vicinity of the obturator lymph nodes which are located inside the acetabula; with a short vagina (age or disease) it is in the lower part where there are no lymph nodes.

TABLE I

FIVE YEAR APPARENT RECOVERY RATES FOLLOWING TREATMENT FOR CARCINOMA OF THE CERVIX AT VARIOUS CENTERS

Institution	Stage I (Per Cent)	Stage II (Per Cent)
Manchester (Christie Hospital)[1]	69.5	46.6
Houston (M. D. Anderson)[1]	86.6	69.9
Stockholm (Radiumhemmet)[1]	86.4	60.0
University of Maryland[3]	87.0	70.0
Puerto Rico Nuclear Center[15]	91.0	63.0

Table II compares local recurrence rates at the Queensland Radium Institute[4] with use of the Manchester system, with results from M. D. Anderson Hospital and the University of Maryland Hospital. Even when the standard system is used these rates are high, being even higher when the treatment is nonstandard, *e.g.*, with a short intrauterine tube, with use of ovoids in any position or combination other than the lateral fornices, or in the absence of an intrauterine tube. By contrast, whole pelvis irradiation[9] prior to intracavitary radium yields excellent local and pelvic control in

TABLE II

COMPARISON OF RECURRENCE RATES

Stage	Queensland Radium Institute Local Recurrences in the Pelvis (Per Cent)		M. D. Anderson Hospital[19] All Cases Failures in the Irradiated Area* (Per Cent)	M. D. Anderson Hospital[7] All Cases Central Recurrences† (Per Cent)	University of Maryland Hospital[3] All Cases Central Recurrences (Per Cent)
I	17.5		4.2	1.8	1.9
	Standard‡	Nonstandard			
Per Cent	13.5	27.0			
II	41.0		12.0	5.7	7.5
	Standard‡	Nonstandard			
Per Cent	34.0	57.0			

* Central failures, pelvic disease, and also disease in the regional lymphatics which are actually not located in the true pelvis.

† Central recurrent disease is defined as clinical or biopsy evidence of persistent or recurrent disease either on the cervix, in the body of the uterus, or in the upper two-thirds of the vagina at any time of follow-up.

‡ Standard Manchester system.

patients with narrow vaults, bulky, barrel-shaped, etc., lesions, the incidence of failures in the irradiated area being 10 per cent in Stage I and 16 per cent in Stage II.

Sherman[21] reported that in 18 cases of carcinoma of the cervix which recurred after intracavitary irradiation, the recurrence was located in a low-dose area. Such "cold spots" often occur with wide separation of the vaginal applicators, even when the standard 8,000 r of the Manchester system is delivered to Point A, or when vaginal colpostats lie anteriorly, producing a "cold spot" on the posterior lip. This demonstrates a direct relationship between "cold spots" and recurrent disease.

COMPLICATIONS

The significance of Point A as a *locus minoris resistentiae* for damage to pelvic structures has no foundation. It has been demonstrated by Lewis *et al.*[14] that Point A, although intended to represent the crossing of the uterine artery and ureter, does not maintain a constant relationship to any specific structure. Its position varies with the type of applicator, individual tumor anatomy, and age of the patient. Thus, in a younger woman Point A lies high in the pelvis, while in an older woman it will lie quite low. Fletcher and associates[8] similarly reported a lack of correlation between dose at Point A, local cure rates, and bladder or rectal complications.

A review of the various complications shows that the contributing factors have no correlation with the dose in the paracervical area (*i.e.*, Point A).

BLADDER

High-dose effects in the bladder are generally associated with proximity of the bladder floor to the radium sources. In marked uterine anteflexion, when the tandem is wrapped around the bladder, the risk of bladder complications is higher. The dose to the bladder varies with the type of vaginal applicators, being high with the Stockholm plaques.

URETERAL STRICTURE

This arises only exceptionally as a complication of irradiation, and is usually caused by direct tumor spread.[5,12]

RECTAL ULCER

Rectal ulcers arise from overdosage to the anterior rectal wall at the level of the posterior fornix and cervix. A central linear source arrangement, used because of a nar-

row vault or with uterine retroposition, is associated with an increased incidence of rectal ulcers.[22]

NECROSIS OF THE VAGINAL VAULT

Necrosis of the vaginal vault, as a rule a self-healing complication, is directly related to mucosal dose. It is primarily associated with small-diameter vaginal applicators which deliver extremely high doses to the mucosa. Here again the lack of correlation of Point A becomes apparent. With the same dose at Point A, a small and compact radium system delivers a higher dose to the mucosa than a large, spread-out system (Fig. 3).

SIGMOIDITIS

Sigmoiditis, always presenting in the loops of the sigmoid colon, is dependent on a number of factors in addition to the amount of external irradiation and intracavitary radium.[11] Some of these factors are: (1) pelvic inflammatory disease or previous surgery which may immobilize the loops of the sigmoid colon and expose the same segment to full-dose irradiation by the radium; (2) the location of the radium system within the pelvis which, if nestled in the hollow of the sacrum, delivers a higher dose to these loops.

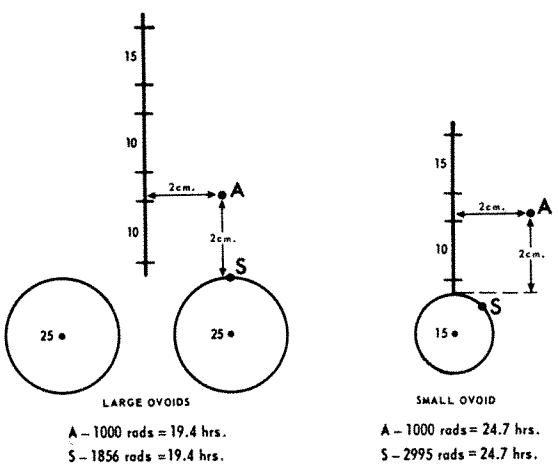


Fig. 3. For delivering 8,000 rads to Point A, the mucosal dose in the vaults increases from 15,000 to 24,000 rads when a compact radium system is used instead of a large one.

The total dose to this region, from external irradiation and intracavitary radium therapy, can best be obtained by adding the dose from whole pelvis irradiation to the contribution by the radium at the periphery of a 10 cm. diameter sphere centered on the center of gravity of the radium system. This can be used as an adequate approximation for tolerance of the sigmoid (Fig. 4). The dose on that sphere is the number of mg. hr. multiplied by 8.25 and divided by 25. Therefore, the only variable is the number of mg. hr. For producing the same dose on that sphere a small radium system delivers a much higher local dose than a large radium system; cases of catastrophic local necrosis have occurred[22] by using large numbers of mg. hr.

DISCUSSION

As a T-shaped or linear arrangement of radioactive sources produces a precipitous fall-off of dose from the surface of the radium applicators to the periphery of the pelvis, there is no "dose" at a point or a surface which is representative of the volume distribution in the pelvis.

Primary intracavitary radium is inadequate except for "non-bulky lesions" with a good local anatomy. The most important consideration is to shrink bulky (≥ 3 cm.), asymmetric, or endocervical cancers prior to radium therapy so as to make the latter effective on the primary tumor. Radium insertions must be spaced at least 2 weeks apart and even longer when more shrinkage is needed or when simultaneous application of tandem and ovoids is not possible because of distorted anatomy. Whole pelvis irradiation makes up for poor anatomy.

The place of external irradiation is not limited to effective treatment of the primary lesion. The incidence of positive lymph nodes from Stage I through Stage III at the time of lymphadenectomy following irradiation is decreased by irradiation.[20] The majority of the regional lymphatics are located outside of the true pelvis[6] (Fig. 2) and cannot be adequately irradiated without external irradiation. Whole pelvis

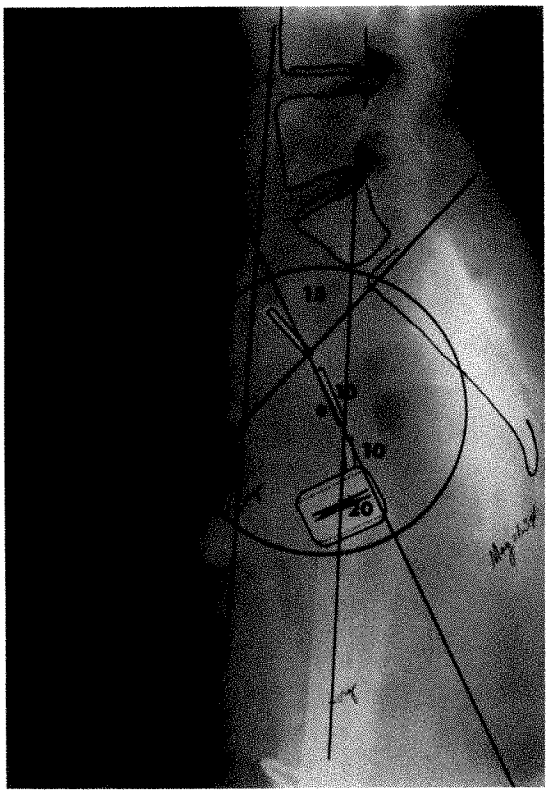


Fig. 4. Pelvic fibrosis and sigmoiditis should be related to the total dose from external irradiation and the dose from intracavitary radium in the hollow of the sacrum obtained by computer dosimetry. The dose calculated on the surface of a sphere 10 cm. in diameter centered over the center of gravity of the radium system would be an adequate approximation for the latter.

For the same number of rads on that sphere, the dose to the tissues in the immediate vicinity of the cervical canal and fornices is much greater with a small radium system than with a large radium system.

For instance:

20 mg., at 1 cm. from midcervix: 100 rads/hr. (or 5 fold)
with 15–10–10
20 mg., at 5 cm. from midcervix: 21 rads/hr.

at 1 cm. from midcervix: 120 rads/hr. (or 10 fold)
with 15–15–25 mg.
at 5 cm. from midcervix: 12.5 rads/hr.

(With permission of *Journal de Radiologie D'Electrologie et de Médecine Nucléaire.*)

and parametrial irradiation fields must be of sufficient height (at least 15 cm.) to encompass the regional lymphatics.

The rules for combining intracavitary radium and external irradiation can only be developed through trial and error and cannot be reduced to a statement of dose from radium at a point or surface. Furthermore, as various types of vaginal applicators have substantially different volume distributions and are used with different dose rates and fractionation schedules, a set of rules cannot be extrapolated from one system to another.

SUMMARY

The results of the treatment of carcinoma of the cervix by the Manchester method are compared with results obtained by other techniques.

The techniques which have yielded superior results have stressed treatment individualization and whole pelvis external irradiation prior to intracavitary radium therapy, when the anatomy is not suitable for the initial delivery of an adequate minimum tumor dose to the periphery of the central tumor by the radium system.

Division of Radiotherapy
Montefiore Hospital and Medical Center
Bronx, New York 10467

REFERENCES

1. Annual report on the results of treatment in carcinoma of uterus and vagina. Annual Report of the International Federation of Gynecology and Obstetrics, 1966, *14*, 65–74.
2. Batley, F., and Constable, W. C. Use of Manchester system for treatment of cancer of uterine cervix with modern after-loading applicators. *J. Canad. A. Radiologists*, 1967, *18*, 396–400.
3. Bloedorn, F. G. University of Maryland Hospital, Baltimore, Maryland. Personal communication, 1968.
4. Bourne, R. G., and Mead, K. W. Proposed method for selecting patients with carcinoma of cervix for radiotherapy or surgery. *Radiology*, 1968, *90*, 139–141.
5. Cantril, S. T. Radiation Therapy in the Man-

agement of Cancer of the Uterine Cervix. Charles C Thomas, Publisher, Springfield, Ill., 1950.

6. DURRANCE, F. Y., and FLETCHER, G. H. Computer calculation of dose contribution to regional lymphatics from gynecological radium insertions. *Radiology*, 1968, *91*, 140–148.
7. DURRANCE, F. Y., FLETCHER, G. H., and RUTLEDGE, F. N. Analysis of central recurrent disease in stages I and II squamous carcinomas of cervix. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED. To be published.
8. FLETCHER, G. H., BROWN, T. C., and RUTLEDGE, F. N. Clinical significance of rectal and bladder dose measurements in radium therapy of cancer of uterine cervix. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1958, *79*, 421–450.
9. FLETCHER, G. H., WATANAVIT, T., and RUTLEDGE, F. N. Whole pelvis irradiation with 4,000 rads in stage I and stage II cancers of uterine cervix. *Radiology*, 1966, *86*, 436–443.
10. FLETCHER, G. H. Textbook of Radiotherapy. Lea & Febiger, Philadelphia, 1966, pp. 434–474.
11. FLETCHER, G. H., and CHASSAGNE, D. Causes possibles des rectosigmoidites survenant après radiothérapie pour cancer du col. *J. de radiol., d' électrol. et de méd. nucléaire*, 1968, *49*, 639–641.
12. KOTTMEIER, H. L. Carcinoma of the Female Genitalia. Williams & Wilkins Company, Baltimore, 1953.
13. KOTTMEIER, H. L. Surgical and radiation treatment of invasive carcinoma of uterine cervix. *Acta obst. et gynec. scandinav.*, 1964, *43*, Suppl. 2.
14. LEWIS, G. C., JR., RAVENTOS, A., and HALE, J. Space dose relationships for points A and B in radium therapy of cancer of uterine cervix. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1960, *83*, 432–446.
15. MARCIAL, V. A. Puerto Rico Nuclear Center. Personal communication, 1968.
16. PATERSON, R. Studies in optimum dosage. *Brit. J. Radiol.*, 1952, *25*, 505–516.
17. PATERSON, R. Clinical trials in malignant disease. Part VI. *Clin. Radiol.*, 1962, *13*, 313–315.
18. PATERSON, R. Clinical trials in malignant disease. Part VIII. *Clin. Radiol.*, 1963, *14*, 17–19.
19. PAUNIER, J.-P., DELCLOS, L., and FLETCHER, G. H. Causes, time of death, and sites of failure in squamous cell carcinoma of uterine cervix on intact uterus. *Radiology*, 1967, *88*, 555–562.
20. RUTLEDGE, F. N., FLETCHER, G. H., and MACDONALD, E. J. Pelvic lymphadenectomy as an adjunct to radiation therapy in treatment for cancer of cervix. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1965, *93*, 607–614.
21. SHERMAN, A. I. Study of radiation failures and role of radioresistance in treatment of cancer of cervix. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1961, *85*, 466–478.
22. STROCKBINE, M. F., HANCOCK, J. E., and FLETCHER, G. H. Complications in 831 patients with squamous cell carcinoma of intact uterine cervix treated with 3,000 rads or more whole pelvic irradiation. To be published.
23. TOD, M. C., and MEREDITH, W. J. Dosage system for use in treatment of cancer of uterine cervix. *Brit. J. Radiol.*, 1938, *11*, 809–823.
24. TOD, M. C., and MEREDITH, W. J. Treatment of cancer of cervix uteri: revised "Manchester method." *Brit. J. Radiol.*, 1953, *26*, 252–257.

THE COMBINATION OF EXTERNAL IRRADIATION AND CURIETHERAPY USED PREOPERATIVELY IN ADENOCARCINOMA OF THE ENDOMETRIUM*

By VICTOR A. MARCIAL, JOSÉ M. TOMÉ, *and* JEANNIE UBIÑAS
SAN JUAN, PUERTO RICO

CARCINOMA of the endometrium is a form of cancer of increasing importance in highly developed communities; as we increase the measures to diminish the morbidity from invasive carcinoma of the cervix, endometrial cancer will gradually become the predominant form of gynecologic cancer. In Puerto Rico carcinoma of the uterine cervix has been and continues to be the number one form of cancer in women; however, carcinoma of the endometrium is increasing in incidence, as observed in the data from the Puerto Rico Cancer Registry[10] and in the experience at the I. González Martínez Oncologic Hospital. In 1956 only 4 cases of carcinoma of the endometrium were registered at the I. González Martínez Oncologic Hospital, whereas in 1966 a total of 28 cases were seen. The reported incidence of cancer of the endometrium (excluding choriocarcinoma) at the Puerto Rico Cancer Registry for the year 1965 was 2.9 cases/100,000 women. Table 1 shows the ratio of cervical cancer to endometrial carcinoma cases as observed at the Puerto Rico Cancer Registry and at the I. González Martínez Oncologic Hospital during the years 1958–1966. We believe that the hospital data regarding accuracy of diagnosis are more reliable in differentiating cervical carcinoma from endometrial carcinoma. This ratio at the Hospital ranged from 18 to 1 in 1958, to 5 to 1 in 1966; we believe that this is a reflection of the changing age and socio-economic patterns of the Puerto Rican population. It is to be expected that as the average age of our female population rises and our socio-economic level improves, together with a reduction in parity we will observe a reduction in incidence of invasive carcinoma of the cervix and a relative increase in endometrial carcinoma to approach a ratio of 1 to 1 between these two conditions. One of us (V.A.M.) has previously reported on the socio-economic aspects of the incidence of cancer in Puerto Rico and has pointed out that carcinoma of the endometrium is more frequently seen in the higher socio-economic groups of women.[9]

TABLE I

RATIO OF CARCINOMA OF CERVIX UTERI TO CARCINOMA OF CORPUS UTERI CASES

	Puerto Rico Cancer Registry	I. González Martínez Hospital
1958	10:1	18:1
1959	13:1	17:1
1960	16:1	17:1
1961	13:1	10:1
1962	16:1	28:1
1963	16:1	14:1
1964	13:1	9:1
1965	14:1	10:1
1966	10:1	5:1

The role of radiation therapy in the management of carcinoma of the endometrium has been considerably debated in the medical literature; the opinions vary from a complete rejection of this modality in the early operable cases[4] to its acceptance as the primary treatment of adenocarcinoma of the endometrium.[7] The majority of reports in the literature consider radiation therapy of great value as an adjuvant to surgery in the management of this form

* Presented at the Fiftieth Annual Meeting of the American Radium Society, Miami Beach, Florida, April 7–11, 1968.
From the Radiotherapy and Cancer Division of the Puerto Rico Nuclear Center, the Radiotherapy Department of the I. González Martínez Hospital, and the University of Puerto Rico School of Medicine, San Juan, Puerto Rico.
This work was supported in part by Public Health Service Grant No. T1-CA-5169-04.

of cancer. Kottmeier,[7] in his compilation of the international results of treatment of cancer of the uterus for the years 1951–60, reported that out of 42 reporting centers in 20 institutions preoperative radiotherapy was applied as a rule, while 21 centers used surgery without preoperative irradiation for tumors limited to the uterus in good surgical risk cases.

The purpose of this report is to present the experience with radiation therapy for this condition at the I. González Martínez Oncologic Hospital, with emphasis on the combination of external and intracavitary irradiation in the preoperative treatment.

MATERIAL

During the period January 1, 1956 to December 31, 1966 a total of 105 not previously treated cases of carcinoma of the endometrium were treated at the Radiotherapy Department of the I. González Martínez Oncologic Hospital. During the same period 28 patients received postoperative irradiation after surgery outside our Hospital, 2 cases were not treated because of critical health, and 1 case was submitted to surgery only, because carcinoma of the cervix had been treated by irradiation several years before. Three cases with sarcoma of the uterus and 5 patients with carcinoma *in situ* or questionable diagnoses were also excluded.

Our institution receives charity patients from a geographic area corresponding to two-thirds of the island of Puerto Rico, with a great concentration on radiotherapeutic cases. Although the number of private cases in the institution has usually been less than 10 per cent of the total work load during the study period, the percentage of private cases in this series was 46 per cent (Table II).

TABLE II

CARCINOMA OF ENDOMETRIUM
SOCIO-ECONOMIC STATUS

	No. of Cases	Per Cent
Indigent	57	54
Nonindigent	48	46
Total	105	100

TABLE III

CARCINOMA OF ENDOMETRIUM
AGE DISTRIBUTION

Age Group	No. of Cases	Per Cent
30–39	4	4
40–49	16	15
50–59	38	36
60–69	26	25
70–79	16	15
80–89	5	5
Total	105	100

Median age—58.7 Youngest—30 yr. of age
Average age—59.7 Oldest—87 yr. of age

The age distribution of this group of cases is shown in Table III; the largest group was constituted by patients 50 to 59 years of age with a median age of 58.7 and an average age of 59.7. The youngest patient was 30 years of age and the oldest 87.

Parity of these cases is shown in Table IV. It is observed that 32 per cent of the women reported had no children and 27 per cent had 1 or 2 children only. This is considered low for the Puerto Rican community, where fertility in women is high.

The menopausal status of women in the study is shown in Table V; only 20 per cent

TABLE IV

CARCINOMA OF ENDOMETRIUM
PARITY

Para	No. of Cases	Per Cent
0	34	32
1–2	28	27
3–4	13	12
5–6	8	8
7–8	8	8
9–	14	13
Total	105	100

TABLE V

CARCINOMA OF ENDOMETRIUM
MENOPAUSAL STATUS

	No. of Cases	Per Cent
Premenopausal	84	80
Postmenopausal	21	20
Total	105	100

of the cases were considered postmenopausal.

The associated medical conditions encountered are shown in Table VI. A complicating medical condition was not mentioned in the chart in only 38 per cent of the cases. The following associated medical conditions were reported in order of diminishing frequency: obesity, hypertension, and diabetes.

For the purpose of classification of extent of the disease, we have used the staging system adopted by the International Federation of Obstetrics and Gynecology in January, 1961. This is as follows: Stage I—the carcinoma is confined to the corpus uteri; Stage II—the carcinoma has involved the corpus and the cervix; Stage III—the carcinoma has extended outside the uterus but not outside the true pelvis; Stage IV—the carcinoma has extended outside the true pelvis or has obviously involved the mucosa of the bladder or rectum. Table VII shows the stage distribution of the cases in the study; the largest number is constituted by the Stage I category, with 72 per cent of the patients. A fractional curettage was not done in the majority of patients that we have classified as Stage I, for the initial diagnostic dilation and curettage was frequently done outside of our Hospital. Consequently, an unknown number of cases with endocervical extent of the disease must have been included in the Stage I group of patients. All cases classified as Stage II had histologic evidence of involvement of the endocervix by carcinoma. The size of the uterus could not be properly evaluated in a significant number of our cases because of associated obesity.

TABLE VI

CARCINOMA OF ENDOMETRIUM
ASSOCIATED MEDICAL CONDITIONS

	No. of Cases	Per Cent
Obesity	15	14
Obesity and hypertension	15	14
Obesity and diabetes	7	7
Obesity, diabetes, and hypertension	12	11
Hypertension	8	8
Hypertension and diabetes	2	2
Diabetes	6	6
Subtotal	65	62
None stated	40	38
Total	105	100

All patients had histologic proof of the disease. In 80 per cent of the cases the diagnosis was reported as adenocarcinoma without reference to grading, and in 10 per cent of the cases this was reported as Grade 2, 3 or anaplastic carcinoma. The diagnosis of adenoacanthoma was made in 4 cases and carcinosarcoma in 1 case.

TREATMENT POLICY

Our treatment policy throughout the years has been to administer preoperative irradiation to all stages of carcinoma of the endometrium and then to follow this by total hysterectomy, approximately 6 weeks after irradiation. Cases who have had primary surgery elsewhere have been accepted for postoperative irradiation but were not

TABLE VII

CARCINOMA OF ENDOMETRIUM
STAGE DISTRIBUTION

Stage	No. of Cases	Per Cent
I	76	72
II	16	15
III	10	10
IV	3	3
Total	105	100

included in this study. When a patient has been considered inoperable she has been submitted to irradiation only by intracavitary curietherapy, by external irradiation or by a combination of both modalities. In the early years covered by this study the preferred form of preoperative irradiation was intracavitary curietherapy, usually by means of the Heyman capsules and a vaginal applicator, for a total of 6,000 to 8,000 mg. hr. Gradually throughout the years we adopted the policy of employing a combination of preoperative irradiation followed by intracavitary curietherapy and preserved curietherapy alone for the very obese patients; in the last 3 years of the study only 3 patients received preoperative curietherapy, while 38 were submitted to preoperative external irradiation followed by curietherapy.

Table VIII shows the distribution of cases by irradiation modality and stage. Preoperative external irradiation followed by intracavitary curietherapy was used in 58 cases and preoperative curietherapy was employed in 22 cases. Fourteen cases had a combination of external and intracavitary irradiation without subsequent surgery. Five cases had intracavitary curietherapy as the only form of therapy. In 3 cases postoperative irradiation was administered in view of the findings in the operative specimen, after previous preoperative curietherapy. Three cases were submitted to external irradiation only.

IRRADIATION TECHNIQUES

In the early years covered by the study the external irradiation was administered by orthovoltage x rays of 250 kvp., a half-value layer of 3 mm. of Cu, a treatment distance of 70 cm., and by a combination of anterior, posterior, and sacrosciatic fields, with exposures of 4,000 r calculated in the mid-pelvis. Since 1958 most cases have been treated with an "El Dorado" cobalt 60 teletherapy unit with a treatment distance of 80 to 100 cm., anterior and posterior fields 16×12 or 16×14 cm. Some cases have been treated with a rotational technique utilizing a Jr. Theratron cobalt 60 teletherapy unit with a 15×15 cm. field. The preferred exposure with cobalt 60 teletherapy has been 5,000 r calculated in the mid-pelvis region administered over a period of approximately 45 days. The fractionation employed has been 5 exposures per week of 150 r each, or 3 exposures of 250 r each per week. The external irradiation has been followed by intracavitary curietherapy by means of a long linear source constituted by four to six 10 mg. sources of radium or a substitute radioisotope such as Co^{60} or Cs^{137} in a tandem arrangement within a plastic or a metal tube to cover the uterine cavity and the upper half of the

TABLE VIII

CARCINOMA OF ENDOMETRIUM
RADIATION THERAPY MODALITY AND STAGE

	Stage				Total
	I	II	III	IV	
Preoperative external and intracavitary irradiation	41	11	6	—	58
Preoperative intracavitary irradiation	18	3	1	—	22
External and intracavitary irradiation only	10	1	2	1	14
Intracavitary irradiation only	5	—	—	—	5
Preoperative intracavitary and postoperative irradiation	2	1	—	—	3
External irradiation only	—	—	1	2	3
Total	76	16	10	3	105

TABLE IX

CARCINOMA OF ENDOMETRIUM
3 YEAR SURVIVAL BY STAGE AND TREATMENT

	Stage								Total	
	I		II		III		IV			
	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.		No.	Per Cent
Preoperative external and intracavitary irradiation	18/21	86	5/7	71	4/5		—		27/33	82
Preoperative intracavitary irradiation	12/17	70	3/3		1/1		—		16/21	76
External and intracavitary irradiation only	1/4		0/1		0/1		0/1		1/7	14
Intracavitary irradiation only	3/4		—		—		—		3/4	
Preoperative intracavitary and postoperative irradiation	2/2		1/1		—		—		3/3	
External irradiation only	—		—		0/1		0/2		0/3	
Total	36/48	75	9/12	75	5/8	62	0/3		50/71	70

vagina. Curietherapy doses have been calculated at a point 2 cm. from the center of the linear source, with a preferred exposure of 3,000 r.

TREATMENT RESULTS

For the purpose of evaluating the results of treatment in this study, we have limited the analysis to cases with a minimal follow-up period of 3 years. Survival results have been determined at 3 and 5 years. Follow-up information is available on all cases.

Table IX shows the 3 year survival by stage and treatment modality in 71 cases that qualify for this analysis. The largest group (33 cases) was submitted to preoperative external and intracavitary irradiation. The 3 year survival for the group was 82 per cent, with a Stage I survival of 86 per cent in 21 cases. Preoperative intracavitary curietherapy was administered to 21 cases with a resulting 3 year survival of 76 per cent; in 17 Stage I cases the 3 year survival was 70 per cent. Other subgroups submitted to irradiation are shown in Table IX. The over-all 3 year survival for all Stage I cases (48) was 75 per cent and the same for 12 Stage II patients. Stage III patients had 3 year survival in 5 out of 8 cases. The over-all 3 year survival for the entire group of 71 patients was 70 per cent. No Stage IV patient survived 3 years.

The 5 year survival by stage and treatment is shown in Table X. The highest survival was observed in the group submitted to preoperative external irradiation and intracavitary curietherapy, with 75 per cent of 16 cases surviving at the end of 5 years. The over-all survival in 49 cases qualifying for 5 year evaluation is 59 per cent. Noteworthy is the fact that 7 of the 49 patients died of intercurrent disease before the end of 5 years; correcting for this we have a net 5 year survival of 69 per cent. The causes of failure at the end of 5 years are shown in Table XI. Only 1 case was alive with disease at 5 years.

The effectiveness of the various modalities of irradiation in eliminating the tumor from the surgical specimen can be observed in Table XII. More than 50 per cent of the removed specimens did not have recognizable tumor on histologic examination. We must emphasize the fact that several pathologists were involved in the examination of these specimens (some from outside our institution) and that no effort was made to review the corresponding histopathology

TABLE X

CARCINOMA OF ENDOMETRIUM
5 YEAR SURVIVAL BY STAGE AND TREATMENT

	Stage								Total	
	I		II		III		IV			
	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.		No.	Per Cent
Preoperative external and intracavitary irradiation	6/8	75	2/3		4/5		—		12/16	75
Preoperative intracavitary irradiation	9/15	60	3/3		1/1		—		13/19	68
External and intracavitary irradiation only	1/3		0/1		0/1		0/1		1/6	17
Intracavitary irradiation only	1/3		—		—		—		1/3	
Preoperative intracavitary and postoperative irradiation	1/2		1/1		—		—		2/3	
External irradiation only	—		—		0/1		0/1		0/2	
Total	18/31	58	6/8	75	5/8	62	0/2		29/49	59

slides by a single pathologist. An analysis of the time interval between irradiation and surgery did not show the relationship between the length of time and the presence or absence of tumor in the specimen. The majority of cases had the uterus removed 4 weeks or more after irradiation. Likewise, no relationship was found between the presence or absence of tumor in the specimen and survival.

The employed irradiation techniques have resulted in no significant morbidity or complications. Postsurgical healing took place uneventfully in all cases.

TABLE XI

CARCINOMA OF ENDOMETRIUM
ANALYSIS OF 5 YEAR FAILURES

Irradiation	Alive 5 Years with Disease	Died with Disease				Died, Cause Unknown	Died, Intercurrent Disease
	Stage	Stage				Stage	Stage
	I	I	II	III	IV	I	I
Preoperative external and intracavitary irradiation	–	2	1	1	–	–	–
Preoperative intracavitary irradiation	1	3	–	–	–	1	2
External and intracavitary irradiation only	–	–	1	1	1	–	2
Intracavitary irradiation only	–	–	–	–	–	–	2
Preoperative intracavitary and postoperative external irradiation	–	–	–	–	–	–	1
External irradiation only	–	–	–	1	1	–	–
Total	1	5	2	3	2	1	7

TABLE XII

CARCINOMA OF ENDOMETRIUM

EFFECTIVENESS OF RADIATION THERAPY TECHNIQUE, BY STAGE

	Stage				Total
	I	II	III	IV	
Preoperative External and Intracavitary Irradiation					
Tumor present	12	2	1	—	15
Tumor absent	9	5	4	—	18
Preoperative Intracavitary Irradiation*					
Tumor present	7	2	1	—	10
Tumor absent	11	2	0	—	13
	—	—	—	—	—
Total					
Tumor present	19	4	2	—	25
Tumor absent	20	7	4	—	31

* Excluding 1 case, Stage I with no pathologic report of surgical specimen.

DISCUSSION

The modest number of cases in this series makes it impossible to arrive at statistically valid conclusions regarding the factors of importance in determining the prognosis of carcinoma of the endometrium. Nevertheless, there are some striking findings that deserve discussion. One of these concerns the similarity in survival results obtained in the Stage I and II cases, and in the Stage III cases. This may be attributable to the whole-pelvis technique of external irradiation employed. Extension of the tumor into the endocervix resulted in a 3 and 5 year survival of 75 per cent in 12 and 8 cases, respectively. Gusberg and Yannopoulos[6] have reported a 27.3 per cent 5 year survival in 14 cases with this type of tumor extension. Davis[4] has also reported a low 5 year survival of 24 per cent in endometrial carcinoma involving the cervix and endocervix.

Taking into consideration that regional lymph node metastases have been reported as high as 20 per cent[11] and that a significant number of cases with endometrial carcinoma tend to metastasize to the ovary, it makes sense to employ a preoperative technique that would irradiate all points in the pelvis to a significant dosage. For this purpose we have utilized external irradiation followed by curietherapy by means of a long linear source. Adequate irradiation of the uterus and the entire pelvis, with precise dosimetry, is afforded by this technique. This technique has achieved sterilization of the tumor from the specimen in over 50 per cent of the cases. Lampe[8] has reported that roentgen irradiation followed by radium gave a 53 per cent sterilization of the tumor in the removed specimen *versus* 28 per cent by roentgen irradiation alone and 32 per cent for preoperative radium.

No vaginal metastases were noted during the first 5 years post-treatment in this series; however, 2 cases developed massive pelvic recurrent carcinoma, one, 10 years post-treatment. The reported incidence of vaginal metastases in nonirradiated cases has been 5 to 17.7 per cent.[13]

No correlation between histologic type of the tumor, size of the tumor and age of patients, and prognosis, could be found in our cases. This could be due to the limited size of our clinical sample. We are left with a number of unanswered questions.

IS RADIATION THERAPY INDICATED AS THE PRIMARY TREATMENT OF CARCINOMA OF THE ENDOMETRIUM?

Table XIII shows the international results of treatment of carcinoma of the corpus reported by Kottmeier for the years 1951 to

1960.[7] The over-all 5 year recovery rate for 14,796 patients (excluding 1,001 cases with endocervical extent) was 62.6 per cent in 42 institutions. The 5 year disease-free survival in the Stage I, Group 1 cases, which are the cases with disease confined to the uterus and constituting a good surgical risk, was 77.1 per cent. On page 401 of the report, the editor states that it is of interest that at 20 institutions reporting 3,985 cases of Stage I, Group 1 in which, as a rule, preoperative irradiation was applied, the 5 year recovery rate was 73.8 per cent, while for 21 institutions reporting 4,668 cases of Stage I, Group 1 in which, as a rule, surgery was performed without preoperative irradiation, the corresponding figure was 76.2 per cent. In an effort to determine the value of irradiation in carcinoma of the corpus, we have prepared Table XIV, based on the reported international results for the years 1951–1960. This table takes into consideration all patients that were registered with a view for treatment at each of the reporting institutions and the survival results were determined using the entire examined population as a basis and not just the cases that were submitted to therapy, as is shown in Table XIII. We expect that if a given treatment influences the outcome of cancer cases seen at an institution, this should reflect on the survival results of the entire group; consequently, the survival analysis should not be limited to a selected group disregarding the fate of the rest of the cases.

TABLE XIII

CARCINOMA OF THE CORPUS
INTERNATIONAL RESULTS OF TREATMENT
1951–60

Stage	No. of Cases	Per Cent 5 Year Recovery Rate
I Group 1	8,963	77.1
I Group 2	3,850	47.1
II	1,983	26.3
	14,796*	62.6

* 1,001 cases with endocervical extent are not included.

TABLE XIV

CARCINOMA OF THE CORPUS
INTERNATIONAL RESULTS RELATED TO TREATMENT
1951–60

	Patients Registered†	Well 5 Years	
		No.	Per Cent
Irradiation	1,373	614	45
Irradiation and surgery	4,491	2,962	66
Surgery—over 50 per cent of cases	6,436	3,894	60
Surgery—less than 50 per cent of cases	3,238	1,791	55
	15,538*	9,261	60

* Includes untreated cases; excludes cases with endocervical extent.
† With a view to treatment.

The first treatment modality presented in Table XIV is radiation therapy. A total of 1,373 patients were registered in 4 institutions utilizing this modality as the primary treatment for carcinoma of the corpus. The lowest 5 year recovery rate was 40 per cent, the highest was 63 per cent with 45 per cent of patients well at the end of 5 years, out of the 1,772 registered cases. Irradiation given preoperatively followed by surgery was utilized on 4,498 patients at 12 institutions with a 66 per cent 5 year recovery rate, which is the highest of all types of treatment; the lowest reported recovery rate with this technique was 42 per cent and the highest 74 per cent. Primary surgery with or without postoperative irradiation for over 50 per cent of the cases was reported at 17 centers, with a 60 per cent 5 year recovery rate in 6,436 cases; the lowest 5 year recovery rate for this category was 44 per cent and the highest 71 per cent. When surgery was employed for less than 50 per cent of the cases (9 centers) the 5 year recovery rate was 55 per cent in 3,238 cases; the lowest 5 year recovery rate in this category was 38 per cent and the highest 72 per cent. Based on these data one can conclude that primary surgery (without preoperative irradiation) for a selected number of cases does not improve the curability in the en-

tire patient population seen at an institution; preoperative irradiation for all cases affords a better chance of curability for the entire group. Radiation therapy alone as the primary treatment of this disease does not achieve as good results as the other modalities of therapy mentioned in Table XIV.

A. OPTIMAL PREOPERATIVE IRRADIATION

The majority of centers utilize intracavitary curietherapy as the preferred technique for preoperative irradiation of carcinoma of the endometrium; this form of therapy affords a satisfactory rate of tumor disappearance and is more expeditious than external irradiation. The Heyman's packing technique seems to be preferred to a single linear source; however, Fletcher[5] considers that when the uterine cavity shows no gross irregularities and the uterus is of normal size, a tandem is better than the Heyman's packing technique. We have found the tandem technique quite satisfactory, particularly after external irradiation, for it permits accurate dosimetry in the irradiated volume. Carmichael and Bean[3] have found that Heyman's packing technique *versus* tandem offers no advantage, but in their hands they observe 10 per cent less specimens with residual tumor with the former. However, no difference is noted in the 5 year survival. Lampe[8] and Sala and del Regato[14] have advocated external irradiation as the preferred form of preoperative irradiation for carcinoma of the endometrium. As previously stated, we have preferred a combination of external irradiation and intracavitary curietherapy as the optimal technique for preoperative irradiation of this condition.

Significance of tumor disappearance. Arneson[1] has stated that an irradiation technique that will increase the incidence of "control" will advance the recovery of patients. Lampe[8] does not believe that total eradication of the neoplasm is necessary before hysterectomy to achieve survival; in a group of 87 patients with residual carcinoma he obtained 92 per cent 5 year survival. Roentgen irradiation alone gave him a 28 per cent sterilization rate with a resulting 5 year survival of 90.1 per cent. We found no difference in the 5 year results in the group of patients with persistent tumor *versus* the group where the tumor disappeared completely after preoperative irradiation.

B. INTERVAL BETWEEN IRRADIATION AND SURGERY

Surgery performed a few days after the termination of radiation therapy would result in a high percentage of persistent tumor in the specimen, but if practiced 6 to 8 weeks after radiation therapy most of the expected tumor disappearance would have occurred. Intervals longer than 2 to 3 months between preoperative irradiation and surgery would be expected to permit tumor regrowth in cases where complete neoplastic sterilization did not occur. We have considered an interval of 6 to 8 weeks as the optimal time for surgery after irradiation with the stated technique; by this time normal tissue radiation induced reactions have subsided and uterine tumoral enlargement has been reduced.

SUMMARY

1. The experience with carcinoma of the endometrium at the Radiotherapy Department of the I. González Martínez Oncologic Hospital is presented. A total of 105 patients were seen from January 1, 1956 to December 31, 1966.

2. All patients were submitted to irradiation followed by surgery for operable cases.

3. The preferred form of preoperative irradiation was a combination of external irradiation and intracavitary curietherapy. This achieved tumor disappearance from the operative specimen in over 50 per cent of the cases.

4. The 3 and 5 year survival results have been analyzed and correlated with the stage of the disease and the treatment modalities employed.

5. A net 5 year survival of 69 per cent

was obtained in 49 patients of all stages, who qualified for 5 year evaluation.

6. An analysis of the published international results of treatment of carcinoma of the endometrium gives basis to the conclusion that preoperative irradiation affords the best chance of 5 year disease free survival for all patients with this disease.

Victor A. Marcial
Puerto Rico Nuclear Center
San Juan, Puerto Rico 00935

REFERENCES

1. Arneson, A. N. Long term follow-up observations in corporeal cancer. Janeway Lecture, 1963. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1964, *91*, 3–21.
2. Beck, R. P., Latour, J. P. A., and Bourne, H. B. Treatment of endometrial carcinoma reassessed: comparison of results of 152 cases, 1949 to 1956, with results of 209 cases, 1926 to 1948. *Am. J. Obst. & Gynec.*, 1964, *88*, 178–183.
3. Carmichael, J. A., and Bean, H. A. Carcinoma of endometrium in Saskatchewan: review of 603 cases with suggested scheme of management for patients with Stage I disease and regarded as good surgical risks. *Am. J. Obst. & Gynec.*, 1967, *97*, 294–307.
4. Davis, E. W., Jr. Carcinoma of corpus uteri: study of 525 cases at New York Hospital (1932–1961). *Am. J. Obst. & Gynec.*, 1964, *88*, 163–170.
5. Fletcher, G. Textbook of Radiotherapy. Lea & Febiger, Philadelphia, 1966, p. 490.
6. Gusberg, S. B., and Yannapoulos, D. Therapeutic decisions in corpus cancer. *Am. J. Obst. & Gynec.*, 1964, *88*, 157–162.
7. Kottmeier, H. L. Annual report on the results of treatment in carcinoma of the uterus and vagina. Volume XIV. Stockholm, 1967.
8. Lampe, I. Endometrial carcinoma. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1963, *90*, 1011–1015.
9. Marcial, V. A. Socioeconomic aspects of incidence of cancer in Puerto Rico. *Ann. New York Acad. Sc.*, 1960, *84*, 981–988.
10. Martínez, I. Cancer in Puerto Rico, 1950–1964. Central Cancer Registry. Puerto Rico Department of Health, 1967.
11. Morton, D. G. Carcinoma of endometrium. *California Med.*, 1963, *99*, 252–257.
12. Pratt, J. H., Symmonds, R. E., and Welch, J. S. Vaginal hysterectomy for carcinoma of fundus. *Am. J. Obst. & Gynec.*, 1964, *88*, 1063–1071.
13. Price, J. J., Hahn, G. A., and Rominger, C. J. Vaginal involvement in endometrial carcinoma. *Am. J. Obst. & Gynec.*, 1965, *91*, 1060–1065.
14. Sala, J. M., and del Regato, J. A. Treatment of carcinoma of endometrium. *Radiology*, 1962, *79*, 12–17.

RECURRENT CANCER OF THE CORPUS UTERI*

TECHNIQUES AND RESULTS OF TREATMENT

By AHMED O. BADIB, M.D., SAMUEL S. KUROHARA, M.D., PH.D., ANTONIO A. BEITIA, M.D., *and* JOHN H. WEBSTER, M.D., C.M.,
BUFFALO, NEW YORK

THE anatomic patterns of recurrences, to a large extent, determine the prognosis of patients with recurrent endometrial cancer.[5] Even within selected series of endometrial carcinoma with vaginal recurrence, the site of recurrence, whether upper or lower vaginal, is of prognostic importance. The wide variation in the published 5 year survival rates from experiences, mainly of vaginal recurrences,[1,3,8–13,15] may be due to the difference in proportions of sites of vaginal lesions, the presence of other pelvic involvement and the limited number of patients in most reports.

The present study evaluates the results of the various methods of treatment of recurrence of cancer in the corpus uteri, at the local, regional or distant sites, with an emphasis on the role of the different radiation techniques in their control.

MATERIALS AND METHODS

From January, 1945 through December, 1965, 300 cases of cancer of the corpus uteri were treated at the Roswell Park Memorial Institute for recurrences from a total of 1,408 cases of endometrial cancer. For this report there must have been at least a 6 month interval of complete clinical regression between initial treatment and time of recurrence, judged by a minimum of 2 consecutive follow-up examinations.[5]

The material includes 241 adenocarcinomas, 26 adenoacanthomas, 24 sarcomas and 9 anaplastic tumors. Nine anatomic recurrent patterns, namely: upper vaginal—72 cases, lower vaginal—17 cases, whole vaginal—6 cases, cervical—17 cases, corporeal—34 cases, parametrial—21 cases, multiple pelvic (vaginal and central or lateral pelvic)—45 cases, distant—21 cases and pelvic and distant—34 cases, are presented to evaluated the treatment results for the carcinomas in this material (Table I). The distribution of cases for the sarcomas and anaplastic tumors (33 cases) is as follows: 6, 1, 0, 1, 1, 2, 8, 3 and 11 cases, respectively.

The clinical data were punched on IBM cards and the statistical analysis was done on a 7040 Electronic Digital Computer.

TREATMENT TECHNIQUES

Four modalities were used in the initial treatment of recurrent endometrial cancer. These were: irradiation (230 cases), surgery (20 cases), combined irradiation and surgery (20 cases), and hormone or chemotherapy (30 cases) (Table I).

In the irradiation group, 101 cases received external irradiation only, 62 cases had local radium therapy only and 67 cases were given radium plus external irradiation (Table II).

External radiation therapy was the main technique used in the treatment of the majority of pelvic recurrences and all distant metastases. Whole pelvic irradiation was given through full rotation, parallel opposing fields or multiple converging ports using orthovoltage, supervoltage or colbalt 60 equipment. A total tumor dose throughout the pelvis of 4,000—6,000 rads in 35—40 days was given to previously unirradiated patients and to those who had been treated with intrauterine radium followed by hysterectomy. In peripheral lymph node metastasis (mostly inguinal), the tumor dose used was

* Presented at the Fiftieth Annual Meeting of the American Radium Society, Miami Beach, Florida, April 7–11, 1968.
From the Department of Radiation Therapy, Roswell Park Memorial Institute, Buffalo, New York.

TABLE I

METHODS OF TREATMENT

	Irradiation	Surgery	Combined	Other	Total
		(a) *Recurrent Endometrial Carcinoma*			
Vagina	86	3	6	0	95
Upper	65	2	5	0	72
Lower	15	1	1	0	17
All	6	0	0	0	6
Cervix	14	0	3	0	17
Corpus	20	7	7	0	34
Pelvic	14	4	3	0	21
Multiple pelvic	38	0	1	6	45
Distant	20	1	0	0	21
Pelvic-distant	19	0	0	15	34
		(b) *Recurrent Endometrial Anaplastic Carcinoma and Sarcoma*			
Vagina	3	3	0	1	7
Upper	3	2	0	1	6
Lower	0	1	0	0	1
All	0	0	0	0	0
Cervix	1	0	0	0	1
Corpus	1	0	0	0	1
Pelvic	1	1	0	0	2
Multiple pelvic	5	1	0	2	8
Distant	2	0	0	1	3
Pelvic-distant	6	0	0	5	11
Total No. of Cases	230	20	20	30	300

in the range of 4,000–6,000 rads in 3–5 weeks delivered by a direct single port in most of the cases. For the treatment of bone metastasis, good relief from pain was achieved with tumor doses ranging from 2,000 rads in 5 cycles within 1 week to 3,000 rads in 2 weeks. Transvaginal x-ray treatment for vaginal recurrences was used only in 2 cases with a beam of 0.5 mm. Cu half-value layer to surface doses

TABLE II

IRRADIATION TECHNIQUES

Site	External Irradiation	Radium	Radium and External Irradiation	Total
Vagina	18	41	30	89
Upper	12	34	22	68
Lower	4	5	6	15
All	2	2	2	6
Cervix	4	7	4	15
Corpus	2	14	5	21
Pelvic	12	0	3	15
Multiple pelvic	20	0	23	43
Distant	22	0	0	22
Pelvic-distant	23	0	2	25
Total	101	62	67	230

of 4,500 rads within 3 weeks.

Local treatment with radium was mainly used in the vaginal, cervical and corporeal recurrences. In the first two lesions, radium in tandem, ovoids or plaques was applied to irradiate part or all of the vagina or the cervix according to the site and extent of the lesion treated. The dose given to the vaginal mucosa was 6,000–7,000 rads in one or more applications within 5–7 days, depending on the volume of tissue irradiated. Radium needles and radon seed implants were used in 5 cases of vaginal recurrences giving a tumor dose of 6,000 rads in about 7 days. In recurrences confined to the corpus in cases treated initially by irradiation (Stage I, Group 2) reirradiation using multiple Heyman's radium capsules or a Roswell Park Memorial Institute applicator was used to give 4,500–6,000 rads at 2 cm. from the surface of the endometrium (or lateral to the uterine applicator).

Combined external irradiation and intracavitary radium was used principally in cases with vaginal recurrences associated with parametrial or central pelvic involvement and in some solitary vaginal lesions to give full pelvic irradiation (Table II). External irradiation in these cases was delivered preceding or following radium application using divergent or split field technique, so that the total combined dose did not exceed 8,000–9,000 rads to the vaginal mucosal surface and not less than 4,000 rads to the pelvic wall in 4 to 6 weeks of treatment.

The surgical procedures used in 40 cases in the second and third treatment groups were local excision (vaginectomy and cervicectomy) in 21 cases, total hysterectomy in 14 cases and pelvic exenteration in 5 cases (Table III).

In the fourth treatment group (Table I), hormonal therapy was given in 19 cases using a pure progestin: 17 hydroxyprogesterone caproate (delalutin, Squibb). Nonhormonal chemotherapy was tried in 11 cases using triethylene thiophosphamide (thiotepa, Lederle), nitrogen mustard (mustargen, Mark, Sharp & Dohm), and cyclophosphamide (cytoxan, Mead Johnson). Hormones and chemotherapy were given also in 38 cases of persistent distant and pelvic-distant lesions after failure of irradiation to control them.

RESULTS

The results of treatment are generally presented in terms of crude survival rates

TABLE III

SURGICAL PROCEDURES

Site	Local Excision	Hysterectomy	Exenteration	Total
Vagina	10	0	2	12
Upper*	7	0	2	9
Lower†	3	0	0	3
Cervix‡	3	0	0	3
Corpus§	0	14	0	14
Pelvic‖	7	0	1	8
Distant	1	0	0	1
Multiple pelvic¶	0	0	2	2
Total No. of Cases	21	14	5	40

* Four received preoperative radium and 1 postoperative external irradiation.
† One case received preoperative radium treatment.
‡ The 3 cases received preoperative radium and external irradiation.
§ Seven cases received preoperative radium treatment.
‖ Three of the cases received postoperative external irradiation.
¶ One case received postoperative external irradiation.

TABLE IV

FIVE YEAR SURVIVAL IN ALL TREATMENT MODALITIES

Site	Irradiation		Surgery		Combined		Other		Total	
	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent
Upper vagina	24/63	38	2/4	50	2/4	50	0/1	0	28/72	39
Lower vagina	3/11	27	0/2	0	—	—	—	—	3/13	23
All of vagina	0/6	0	—	—	—	—	—	—	0/6	0
Cervix	6/13	46	—	—	3/3	100	—	—	9/16	56
Corpus	7/19	37	4/7	55	6/6	100	—	—	17/32	53
Pelvic	4/13	31	0/3	0	1/3	33	—	—	5/19	26
Multiple pelvic	7/33	21	0/1	0	0/1	0	0/5	0	7/40	18
Distant	3/19	16	0/1	0	—	—	0/1	0	3/21	14
Pelvic-distant	1/17	6	—	—	—	—	0/13	0	1/30	3
Total	55/194	28	6/18	33	12/17	70	0/20	0	73/249	29

after 5 years from treatment. Statistical tests of hypothesis were used only when the differences in rates appeared large and/or when the number of cases seemed reasonable.

Table IV presents the results of treatment after various methods in the anatomic subgroups of recurrences. In this series, the 5 year survival in the recurrent carcinoma was 32 per cent, and in the anaplastic tumors and sarcoma was 10 per cent (29 per cent in the whole series).

The results of treatment after various radiation techniques in the group treated only by irradiation are given in Table V. Full pelvic irradiation (using external irradiation alone or combined with radium) and local vaginal irradiation (using radium or transvaginal x ray) gave equal results in upper vaginal recurrences. The 5 year survivals were 10/27 (37 per cent) and 13/33 (39 per cent), respectively. Full pelvic irradiation resulted in the only 5 year survival among patients with lower vaginal recurrences: 3/7 (43 per cent) *versus* 0/4 (0 per cent) after local vaginal irradiation. In cervical and corporeal lesions, the results of combined radium

TABLE V

FIVE YEAR SURVIVAL IN VARIOUS IRRADIATION TECHNIQUES

Site	External Irradiation		Radium		Combined		Total	
	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent
Upper vagina	4/11	35	13/34	38	7/18	39	24/63	38
Lower vagina	1/3	33	0/4	0	2/4	50	3/11	27
All of vagina	0/2	0	0/2	0	0/2	0	0/6	0
Cervix	1/3	33	2/7	29	3/4	75	6/14	43
Corpus	0/2	0	4/13	31	3/5	60	7/20	35
Pelvic	3/10	30	—	—	1/3	33	4/13	31
Multiple pelvic	2/15	13	—	—	5/18	28	7/33	21
Distant	3/18	17	—	—	—	—	3/18	17
Pelvic-distant	0/15	0	—	—	1/2	50	1/17	6
Total	14/79	18	19/60	32	22/56	39	55/195	28

TABLE VI

FIVE YEAR SURVIVAL IN SURGICAL AND COMBINED TREATMENT

Site	Local Excision		Hysterectomy		Exenteration		Total	
	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent
Upper vagina	2/6	33	—	—	2/2	100	4/8	50
Lower vagina	0/2	0	—	—	—	—	0/2	0
Cervix	3/3	100	—	—	—	—	3/3	100
Corpus	—	—	10/13	77	—	—	10/13	77
Pelvic	1/5	20	—	—	0/1	0	1/6	17
Multiple pelvic	—	—	—	—	0/2	0	0/2	0
Distant	0/1	0	—	—	—	—	0/1	0
Total	6/17	35	10/13	77	2/5	40	18/35	51

plus external irradiation were superior to those of radium alone or external irradiation (Table v).

The results after surgical treatment and combined irradiation and surgery are given in Table VI. The combined method showed its best results in the cervical stump and corporeal recurrence. All patients in both these groups survived more than 5 years.

In the fourth group, hormones seemed to be more effective in patients with adenoacanthoma and adenocarcinoma giving remission of 2–3 years duration in one-fourth of the patients without toxic effects. Chemotherapy resulted in some subjective improvement but less significant objective response. However, the use of hormones and chemotherapy in recurrent lesions persistent after irradiation did not improve the prognosis.

DISCUSSION

Radiation therapy has been the most commonly used procedure in the management of locally and/or regionally recurrent cases;[8–13] however, radical surgery has been suggested to offer a prolonged survival in selected cases.[2,4] In this series, the surgical procedures varied from local resection of vagina or cervical stump through hysterectomy to pelvic exenteration. In this small number of surgical cases, the survival rates were comparable to those of similar cases treated by irradiation. In Brunschwig's report,[2] 6 cases with localized pelvic recurrence were treated by radical vaginal excision with pelvic lymph node dissection and 33 cases by pelvic exenteration resulting in 28 per cent 5 year survival. The same type of recurrence treated in our series by irradiation resulted in 38 per cent 5 year survival. Pratt[7] stated that only small numbers of recurrent endometrial cancer will be relatively localized to be amenable to surgery. In his series, of 11 recurrences treated by anterior and total exenteration, 2 have survived 5 years. In this material, when surgery followed irradiation in recurrences limited to the corpus and cervical stump, it resulted in a 5 year survival for these patients.

The survival rate in cases with vaginal recurrences after irradiation (34 per cent at 5 years) compares favorably with other published results.[3,8,11] Whole pelvic irradiation seemed to be the treatment of choice in the lower vaginal lesions resulting in better survival. This can be explained by the likelihood that lower vaginal recurrences are usually metastatic rather than a direct extension of the disease and, consequently, metastatic lesions are more likely to exist elsewhere in the pelvis.[7,10] The small number of cases makes it difficult to evaluate the data statistically; nevertheless, the trend was consistent in the 2 year and 5 year survival rates. Therefore, we feel the whole pelvis should be irradiated in such cases. The two radiation

techniques did not produce any difference in results when applied to the upper vaginal lesion. This finding may be related to the possibility that such recurrences may represent implantations of tumor following surgery or direct extension of the primary lesion.[3,8,9]

The concept that the upper vaginal lesions represent localized disease and that lower vaginal recurrence is part of a regional metastatic process is supported by the good results achieved by Dobbie[3] in the treatment of principally upper vaginal lesions with localized radium therapy and the relatively poor results reported in Stander's series,[13] where similar treatment was applied to pricipally lower vaginal recurrences. In this series, cases with lower vaginal recurrences treated by full pelvic irradiation have survived equally with those with lesions in the upper vagina treated with local irradiation.

Full pelvic irradiation used in this material consisted of external irradiation alone or combined with radium application. The number of cases treated by either or both of these radiation techniques in each subgroup of recurrences was relatively small with no statistically significant difference between the 5 year survival rates. However, the data suggest a more frequent control following the combined radiation technique.

Local vaginal irradiation with various types of intracavitary radium application or radium implantation gave equal results in the control of vaginal recurrences. Treatment with radium is usually simple, satisfactory, and the use of intracavitary applicators requires no anesthesia. Del Regato[10] favored transvaginal roentgen therapy as less elaborate and less hazardous, but this method still has limitations, mainly because most vaginal lesions will not fit in the treatment cone and the daily application can be painful after the early appearance of the radiation reaction.

In our experiences, local radium therapy should be limited to the treatment of the true upper vaginal solitary lesion after exclusion of any pelvic involvement. External irradiation is added if the lesion extends to the parametrium or the recurrence involves the lower vagina.

Chemotherapy and hormonal treatment are most often used in advanced recurrences as an initial treatment or as a subsequent measure in recurrences which persist after radiation. Our results corroborate the published reports[6,14] showing their palliative effectiveness with little or no prolongation of life. The hormonal treatment has the advantage of being nontoxic and more effective in the more differentiated lesions of the carcinoma group.

SUMMARY

Three hundred cases of recurrent endometrial cancer were treated initially by irradiation (230 cases), surgery (20 cases), combined irradiation and surgery (20 cases), and hormonal therapy or chemotherapy (30 cases) and the results are reported. Full pelvic irradiation was superior to local vaginal irradiation in lower vaginal metastases.

No such differences were found in those with solitary upper vaginal recurrences where intracavitary radium was equally successful.

Combined irradiation and surgery resulted in the best survival of cases with corporeal and cervical stump recurrences.

In advanced cases, hormonal treatment yielded a 2 year remission rate of 25 per cent, especially in the carcinoma group of recurrences.

Ahmed O. Badib, M.D.
Department of Radiation Therapy
Roswell Park Memorial Institute
Buffalo, New York 14203

REFERENCES

1. BOUTSELIS, J. G., ULLERY, J. C., and BAIR, J. Vaginal metastases following treatment of endometrial carcinoma. *Obst. & Gynec.*, 1963, *21*, 622–626.
2. BRUNSCHWIG, A. Surgical treatment of recurrent endometrial cancer. *Obst. & Gynec.*, 1961, *18*, 272–276.
3. DOBBIE, B. M. W. Vaginal recurrences in carcinoma of body of uterus and their prevention

by radium therapy. *J. Obst. & Gynaec. Brit. Emp.*, 1953, *60*, 702–795.

4. FINN, W. F. Time, site and treatment of recurrences of endometrial carcinoma. *Am. J. Obst. & Gynec.*, 1950, *60*, 773–782.
5. KUROHARA, S. S., BADIB, A. O., WEBSTER, J. H., and BEITIA, A. A., Recurrent cancer of corpus uteri. To be published.
6. PARKER, R. T., NEWTON, Z. B., and PEETE, C. H. Non-hormonal chemotherapy of recurrent endometrial cancer. In: New Concepts in Gynecologic Oncology. F. A. Davis Company, Philadelphia, 1966, pp. 269–273.
7. PRATT, J. H. Surgical treatment of recurrent endometrial carcinoma. In: New Concepts in Gynecologic Oncology. F. A. Davis Company, Philadelphia, 1966, pp. 261–267.
8. PREM, K. A. Adenocarcinoma of endometrium with special reference to vaginal involvement. *Univ. Minnesota M. Bull.*, 1958, 24–29
9. PRICE, J. J., HAHN, G. A., and ROMINGER, C. J. Vaginal involvement in endometrial carcinoma. *Am. J. Obst. & Gynec.*, 1965, *91*, 1060–1965.
10. DEL REGATO, J. A. Radiotherapy in treatment of recurrent carcinoma of endometrium. In: New Concepts in Gynecologic Oncology. F. A. Davis Company, Philadelphia, 1966, pp. 257–260.
11. RUBIN, P., GERLE, R. D., QUICK, R. S., and GREENLAW, R. H. Significance of vaginal recurrence in endometrial carcinoma. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1963, *89*, 91–100.
12. RUTLEDGE, F. N., TAN, S. K., and FLETCHER, G. H. Vaginal metastases from adenocarcinoma of corpus uteri. *Am. J. Obst. & Gynec.*, 1958, *75*, 167–174.
13. STANDER, R. W. Vaginal matastases following treatment of endometrial carcinoma. *Am. J. Obst. & Gynec.*, 1956, *71*, 776–779.
14. VARGA, A., and HENRIKSEN, E. Hormonal treatment of endometrial cancer. In: New Concepts in Gynecologic Oncology. F. A. Davis Company, Philadelphia, 1966, pp. 301–308.
15. WAY, S. Vaginal metastases of carcinoma of body of uterus. *J. Obst. & Gynaec. Brit. Emp.*, 1951, *58*, 553–572.

ADENOCARCINOMA OF THE UTERUS*

By LUIS DELCLOS, M.D., GILBERT H. FLETCHER, M.D., AUGUSTO G. GUTIERREZ, M.D., *and* FELIX N. RUTLEDGE, M.D.
HOUSTON, TEXAS

ADENOCARCINOMA of the uterus can be found after fractional curettage to be limited to the endometrium or the uterine cervix, or to involve both—the so-called corpus et collum, according to Heyman's terminology.[4,5]

As a rule, adenocarcinomas of the cervix are of endocervical origin. They commonly invade the myometrium and may grow to large lesions at the level of the endocervix and isthmus. This pattern of local growth allows them to remain longer in Stages I and II than the squamous cell carcinomas.

The purpose of this paper is to compare the pattern of spread within those 3 categories and with the pattern of spread of squamous cell carcinoma. An analysis of the sites of failure will be done by modalities of treatment to find specific guidelines for treatment of patients with adenocarcinoma of the corpus et collum. Treatment plans for disease limited to only the corpus and only the cervix have been previously described.[2]

CLINICAL MATERIAL

From 1948 through December 1964, 568 patients with previously untreated adenocarcinoma of the uterus were treated at the University of Texas M. D. Anderson Hospital and Tumor Institute at Houston; 321 were classified as endometrial cancer, 106 as cervical cancer, and 141 as corpus et collum cancer (Table I).

There are 3 clinical situations which can be outlined for corpus, corpus et collum, and cervix-only cases: (1) patients with operable lesions and good surgical risks; (2) technically operable lesions but poor surgical risks; and (3) disease too advanced for surgical resection. In the endometrium group the tumor was considered technically unresectable when metastases, including widespread abdominal carcinomatosis, were present. For the corpus et collum and cervix-only group, the reason for unresectability was extension to the lateral parametria, lower vagina, or both (Stages III and IV for adenocarcinoma of the cervix).

TABLE I

ADENOCARCINOMA OF THE UTERUS
PREVIOUSLY UNTREATED PATIENTS
1948 through December 1964

Area of Involvement	No. of Patients Treated
Endometrium	321
Corpus et collum	141
Cervix	106
Total	568

Hysterectomy after irradiation has been performed routinely in the corpus and corpus et collum groups, but not systematically in Stages I and II adenocarcinomas of the cervix.[6]

METHODS OF TREATMENT

The treatment for adenocarcinomas of the cervix has been similar to the treatment for squamous cell carcinomas, with perhaps less emphasis on external irradiation, whether it was parametrial or whole pelvis, in favor of intracavitary radium therapy. For the endometrial cancer, treatment has been primarily intrauterine and intravaginal radium therapy. For the corpus et collum cancers, a specific pattern of irradiation treatment has developed in the last few

* Presented at the Fiftieth Annual Meeting of the American Radium Society, Miami Beach, Florida, April 7–11, 1968.
From the Department of Radiotherapy, and the Department of Surgery, Section of Gynecology, The University of Texas M. D. Anderson Hospital and Tumor Institute at Houston, Houston, Texas.
This investigation was supported by Public Health Service Research Grants No. CA-06294 and CA-05654 from the National Cancer Institute.

years which is closer to the treatment for adenocarcinoma of the cervix than to the treatment for cancer limited to the endometrium only.

The hysterectomy was of the conservative type with lymphadenectomies performed in the early years of the program. In more recent years, lymphadenectomies have been abandoned for all 3 groups.

OPERATIVE FINDINGS

The operative findings are shown in Table II. For the endometrial group, in 7 per cent of the patients, disease has been found in the pelvic structures, *i.e.*, ovaries, tubes, and peritoneal surface of the pelvic cavity. It is also of interest that of 66 lymphadenectomies, only 1 was positive (this patient also had tumor in the pelvic structures). This low incidence of involved regional lymph nodes does not result from the previous irradiation because intracavitary radium alone, used in most patients, contributes little radiation to the regional lymphatics.

In the corpus et collum group, several patients had the pelvic structures involved, primarily the result of implants above the serosal surface of the uterus or pelvic walls with initial lesions apparently of small size. The incidence of positive involvement of regional and para-aortic lymph nodes, although higher than in the endometrium-only group, is still less than for squamous cell carcinoma of the cervix. Twenty-five lymphadenectomies were done and only 2 were positive; in 3 other instances, the regional lymphatics were found to have positive involvement, but it was not worthwhile to do a lymphadenectomy because of unresectable disease, either in the pelvic structures or in the para-aortic lymph nodes. This is a low incidence of involvement of regional lymphatics for a disease that involves the cervix and may partially result from external irradiation, which was given either in the form or parametrial or whole pelvis irradiation.

The incidence of positive lymph nodes in adenocarcinoma of the cervix again is low (2 of 57 patients had positive regional lymph nodes—1 of the 2 also had positive

TABLE II

OPERATIVE FINDINGS (IRRADIATION AND SURGERY)
ADENOCARCINOMA OF THE UTERUS

1948 through December 1964

	Endometrium		Corpus et Collum		Cervix, Stages I and II	
	No. of Patients	Dead of Tumor	No. of Patients	Dead of Tumor	No. of Patients	Dead of Tumor
Negative	145	6	35	2	28	1
Positive uterus only	69	7	33	5	26	5
Positive regional lymphatics only*	0	0	5	3	1	1
Positive pelvic structures*	13†	6	4	3	0	0
Positive para-aortic lymph nodes‡	6§	5	5‖	5	2	2¶
Total	233	24	82	18	57	9

* With or without residual tumor in uterus.
† One had positive regional lymph nodes also.
‡ With or without residual tumor in uterus and/or pelvis.
§ Three had pelvic disease too.
‖ One had pelvic disease and 1 had positive pelvic lymph nodes also.
¶ One had positive pelvic lymph nodes also.

TABLE III

ABSOLUTE SURVIVAL
ADENOCARCINOMA OF THE UTERUS
(PREVIOUSLY UNTREATED PATIENTS)

1948 through December 1964—3 Years
1948 through December 1962—5 Years

	Endometrium		Corpus et Collum		Cervix	
	3 Years	5 Years	3 Years	5 Years	3 Years	5 Years
Resectable						
Good medical risk (irradiation and surgery)*	196/233 (84%)	144/181 (79%)	59/82 (72%)	36/61 (59%)	54/70 (77%)	37/53 (70%)
Poor medical risk (irradiation alone)	41/66 (62%)	35/61 (57%)	16/32 (50%)	10/25 (40%)	6/9 (67%)	5/6 (83%)
Unresectable						
Too advanced for surgery (irradiation alone)	0/22†	0/21	6/27 (22%)	5/26 (19%)	10/27 (27%)	7/26 (27%)

* Except cervix group, where surgery may or may not have been done.
† Twenty patients had distant metastases when first seen.

para-aortic lymph nodes). Of 35 lymphadenectomies for adenocarcinoma of the cervix, only 2 were positive (in 1 instance the para-aortic lymph nodes were also involved). Here again, external irradiation, being given in many instances, is partially responsible for the low incidence of positive lymph nodes, but it also seems that adenocarcinoma of the cervix does not spread as often to the regional lymphatics as does squamous cell carcinoma.

SURVIVAL RATES AND SITES OF FAILURE

The survival rates are tabulated in Table III for the 3 anatomic groups in each of the 3 clinical situations. In the resectable patient groups, the corpus et collum lesions have the poorest survival rates. When the cancer was limited to the endometrium, 20 of 22 patients were inoperable because of existing distant metastases, including diffuse abdominal carcinomatosis.

The survival rates for the unresectable corpus et collum and cervix-only patients, the majority of whom are Stage III, although a few are Stage IV, are poor (19 and 27 per cent). These rates are not as good as those for patients with squamous cell carcinoma in which, for Stage III_A, the survival rates are 45 per cent and, for Stage III_B, 36 per cent. For adenocarcinoma of the cervix Stage III_A, the survival rate is 33 per cent; for Stage III_B it is 11 per cent.[3]

Local control of the disease in the irradiated area for adenocarcinoma of the cervix on an intact uterus is also poor: survival rates are only 46 per cent for Stage III_A and 15 per cent for Stage III_B *versus* 73 and 62 per cent for squamous cell carcinomas.[3]

Table IV reveals the causes of death for all categories. Table V gives the sites of failure for the technically operable cases. The pelvic failures are about the same in the 3 groups. It is worth noting that distant metastasis is the main cause of death by tumor in the corpus et collum group. This includes abdominal carcinomatosis, which can perhaps be explained by tumor invading the myometrium and spreading through the serosa and/or the fallopian tubes to the abdominal cavity.

METHOD OF TREATMENT FOR CORPUS ET COLLUM GROUP AND ENDOMETRIUM-ONLY GROUP

As this pattern of spread became evident through the years, whole pelvis irradiation was given for the endometrial cancers when

TABLE IV

CAUSES OF DEATH—3 YEARS
ADENOCARCINOMA OF THE UTERUS

1948 through December 1964

	No. of Patients	Dead from Disease		Dead from Intercurrent Disease	
		No.	Per Cent	No.	Per Cent
Endometrium					
Good risk	233	**24**	**10**	4	1.5
Poor risk	66	**9**	**14**	9	14
Advanced	22*	19	86	1	5
Corpus et Collum					
Good risk	82	**18**	**22**	1	1
Poor risk	32	**11**	**34**	4	12
Advanced	27	16	60	1	4
Adenocarcinoma of Cervix					
Good risk	70	**12**	**17**	2	3
Poor risk	9	**0**		3	33
Advanced	27	16	60	1	4

* Twenty patients had distant metastases on admission.

the uterus was large and/or the tumor was anaplastic. The techniques for treatment of the endometrium-only group have been published previously.[2]

For corpus et collum cases, whole pelvis irradiation is emphasized for large uterine and/or anaplastic tumors because the chances for the tumor to reach the serosal surface of the uterus are greater. It has been reported previously[1] that whole pelvis irradiation for adenocarcinoma of the fundus and corpus et collum is locally effective with doses from 4,000 to 5,000 rads. Of patients who were not surgical candidates, either because of poor surgical risk or unresectable tumor, 20 of 74 had pelvic recurrences when doses of less than 3,000 rads had been given; 3 of 31 had pelvic recurrences when doses above 3,000 rads were given (in addition to the intrauterine and vaginal radium).

Also, because spread to the vagina and the parametria is similar to that of adenocarcinoma of the cervix, intracavitary radium therapy is of the same type as that used for squamous cell carcinoma of the

TABLE V

TECHNICALLY OPERABLE GROUPS
IRRADIATION AND SURGERY, IRRADIATION ONLY—POOR RISK
ADENOCARCINOMA OF THE UTERUS

1948 through December 1965

	No. of Patients Treated	Failures Within Pelvis		Distant Metastases Only	
		No.	Per Cent	No.	Per Cent
Endometrium	299	21*	9	12	4†
Corpus et Collum	114	13*	11	16	14†
Adenocarcinoma of the Cervix	79	8*	10	4	5

* In 75 per cent of these patients failure was due to involvement of the pelvic structures or the peritoneal surface of the true pelvis.
† Includes abdominal carcinomatosis.

TABLE VI

ADENOCARCINOMA OF THE CORPUS AND CERVIX

(CORPUS ET COLLUM)

Clinical Situation	Whole Pelvis	Uterus	Vagina	Parametria	Comments
Preoperative Irradiation (1) Normal size uterus, well differentiated tumor. No extension beyond uterus or cervix	—	Tandem and ovoids 72–48 hr. 2 weeks apart		3,000–4,000 rads	Hysterectomy to follow in 4–6 weeks
(2) Slightly or moderately enlarged uterus, well differentiated tumor. No extension beyond uterus or cervix	4,000 rads	2,500 mg.-hr. tandem or Heyman packing	72 hr. ovoids	No additional	Hysterectomy to follow in 4–6 weeks
(3) Normal size uterus, anaplastic tumor	4,000 rads	Tandem and ovoids 72 hr. or 48–24 hr. 2 weeks apart		No additional	Hysterectomy to follow in 4–6 weeks
Technically Operable but Surgery Contraindicated (1) Normal size uterus, well differentiated tumor. No extension beyond uterus or cervix	—	Tandem and ovoids 72–72 hr. 2 weeks apart		3,000–4,000 rads	
(2) Slightly or moderately enlarged uterus, well differentiated tumor. No extension beyond uterus or cervix	4,000 rads	2 insertions 3,500–4,000 mg.-hr. 2 weeks apart, Heyman packing or tandem	Ovoids 48–48 hr. 2 weeks apart		
(3) Normal size uterus, anaplastic tumor	4,000 rads	Tandem and ovoids 48–48 hr. 2 weeks apart			
Technically Inoperable (1) Normal size uterus (a) Extension to upper ⅓ of vagina and/or extension to parametria, not fixed to pelvic wall	4,000 rads	Tandem and ovoids 48–48 hr. 2 weeks apart			
(b) Fixed to pelvic wall	5,000 rads	Tandem and ovoids 72 hr. or 48–24 hr. 2 weeks apart		Extra 1,000 rads to one parametrium if slow regression	
(2) Enlarged uterus (a) Extension to upper ⅓ of vagina and/or parametria but not fixed to pelvic wall	4,000 rads	2 insertions 3,500–4,000 mg.-hr. 2 weeks apart, Heyman packing or tandem	Ovoids 48–48 hr. 2 weeks apart		
(b) Fixed to pelvic wall	5,000 rads	Individualize intracavitary radium with tandem and ovoids or Heyman packing and vaginal ovoids or add extra 1,000–2,000 rads through reduced fields			
(c) Massive uterus	5,000 rads				

cervix; whereas in endometrial cancer, vaginal radium is limited to a total surface dose of 8,000 rads in the 2 insertions, unless the patients are clinically unsuitable for surgical therapy. The Heyman packing technique is not used preoperatively, but instead a long tandem is used to give maximum paracervical irradiation in combination with the same type of vaginal radium therapy used for squamous cell carcinoma. If the disease is clinically unresectable and the uterine cavity is enlarged, the Heyman packing technique may be used.

Table VI summarizes the details of tech-

niques of treatment for the corpus et collum cases.

CONCLUSION

Adenocarcinoma of the uterus, originating either in the endometrium or endocervix, grows locally to large size, can spread directly to the pelvic structures, and frequently does not spread to lymph nodes.

Because of the direct spread to the pelvic structures, when the tumor is of significant size or the tumor is anaplastic, increased use of whole pelvis irradiation is indicated.

Luis Delclos, M.D.
Department of Radiotherapy
University of Texas
M. D. Anderson Hospital
and Tumor Institute
Houston, Texas 77025

REFERENCES

1. DELCLOS, L., and FLETCHER, G. H. Malignant tumors of endometrium: evaluation of some aspects of radiotherapy. In: Carcinoma of the Uterus and Ovary. University of Texas M.D. Anderson Hospital and Tumor Institute 11th Annual Clinical Conference. To be published.
2. FLETCHER, G. H. Textbook of Radiotherapy. Lea & Febiger, Philadelphia, 1966.
3. FLETCHER, G. H. Cancer du col uterin, Stade III. *J. de radiol., d'électrol. et de méd. nucléaire*, 1968, *49*, 629–639.
4. HEYMAN, J., REUTERWALL, O., and BENNER, S. Radiumhemmet experience with radiotherapy in cancer of corpus of uterus: classification, method of treatment and results. *Acta radiol.*, 1941, *22*, 14–98.
5. KOTTMEIER, H. L. Carcinoma of corpus: its classification and treatment. *Gynaecologia*, 1954, *138*, 287–310.
6. RUTLEDGE, F. N., GUTIERREZ, A. G., and FLETCHER, G. H. Management of Stage I and II adenocarcinomas of uterine cervix on intact uterus. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1968, *102*, 161–164.

Vol. 105, No. 3

AFTERLOADING VAGINAL OVOIDS*

By ALLAN E. GREEN, Jr., M.D., JOHN R. BROADWATER, M.D.,† *and* JAMES A. HANCOCK, Jr., MAJOR, USAF, B.S.C.‡
MEMPHIS, TENNESSEE

Since 1964 we have used a modification of the Fletcher vaginal ovoids[1,2,3] for radium therapy of gynecologic malignancy. Following the principle of afterloading of radiation sources as described by Henschke,[4] and Suit and co-workers,[5] the ovoid design was altered to permit simplicity of insertion and loading.

The planning, construction, and original use of the modified ovoids were done at Wilford Hall USAF Hospital, Lackland AFB, Texas. The afterloading ovoids have now been employed in over 500 patient applications and are currently in use at 7 institutions.

DESIGN

Having received initial training and experience with the Fletcher vaginal ovoids and convinced of its superiority over other radium applicators for gynecologic use, our first premise in planning design of the afterloading system was to leave unaltered the basic source holder. Accordingly, the density of metallic material, wall thickness, vertical height, diameter, and tungsten blocks in the superior-inferior surfaces remain precisely as in the ovoids originally described by Fletcher and associates[1] (Fig. 1, *A*, *B* and *C*).

Our modifications were directed toward providing the ovoids with the afterloading potential. The solid metal handles were replaced with thin tubing (8 mm. over-all diameter) to reduce the bulkiness of metal that would be lodged in the vagina. A rubber plunger is employed to push the radium source through the tube into the ovoid (Fig. 2). The source drops into a slot in the ovoid by gravity. The source is then held in the exact center of the ovoid by pressure of the rubber plunger and tube capping. This center position of the source has been proven by hundreds of trial insertions of a dummy source and by roentgenography (Fig. 3). The radium tube (or microsource) can be retrieved or afterunloaded from the ovoid by a suture applied to the tube eyelet. A hollow cylindrical carrier was designed for use with needle-type or nonstandard radium tubes. The ovoids can be broken down for cleaning purposes.

RADIATION MEASUREMENTS

As a final check on the exact duplication of the afterloading model with the original Fletcher ovoids, measurements of radiation were performed in phantom materials. Dual testing with a NaI crystal probe in pressdwood and LiF microrods in paraffin resulted in radiation readings as shown in Table 1.

CLINICAL USE

The metal ovoids can be fitted with plastic or teflon sleeves to increase the diameter according to vaginal capacity. As in the Manchester and Fletcher systems, the following ovoid diameters are considered:

Small ovoid	2.0 cm. diameter	No sleeve
Medium ovoid	2.5 cm. diameter	No. 1 sleeve
Large ovoid	3.0 cm. diameter	No. 2 sleeve

In the treatment of carcinoma of the cervix uteri, vaginal ovoids are used in conjunction with uterine tandems of the afterloading type. As described by Suit *et al.*[5] and later modified by Delclos, the uterine afterloading tube is 7 mm. in over-all diameter, is supplied in various angles and curves, and has a metallic collar that can be adjusted to uterine length. Thus, 3 hollow tubes present at the external genitalia

* From the Department of Radiology, Baptist Memorial Hospital, Memphis, Tennessee.
† Present Address: Holt-Krock Clinic, Fort Smith, Arkansas.
‡ Present Address: Malcolm Grow USAF Hospital, Andrews AFB, Maryland.

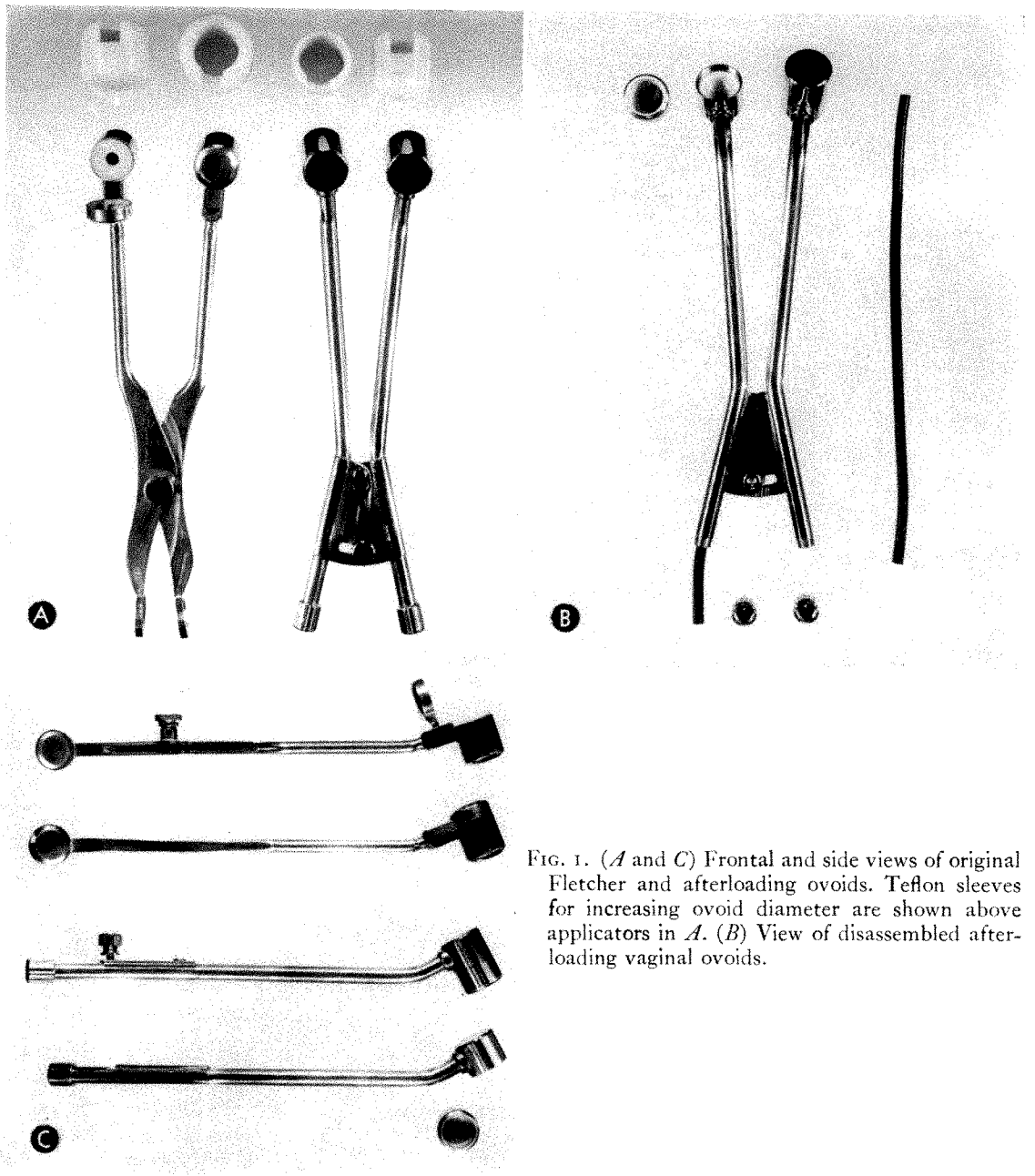
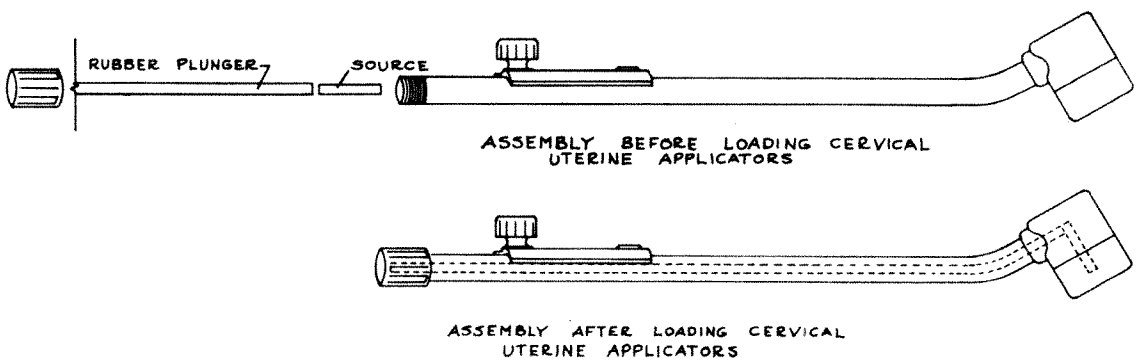


FIG. 1. (*A* and *C*) Frontal and side views of original Fletcher and afterloading ovoids. Teflon sleeves for increasing ovoid diameter are shown above applicators in *A*. (*B*) View of disassembled afterloading vaginal ovoids.



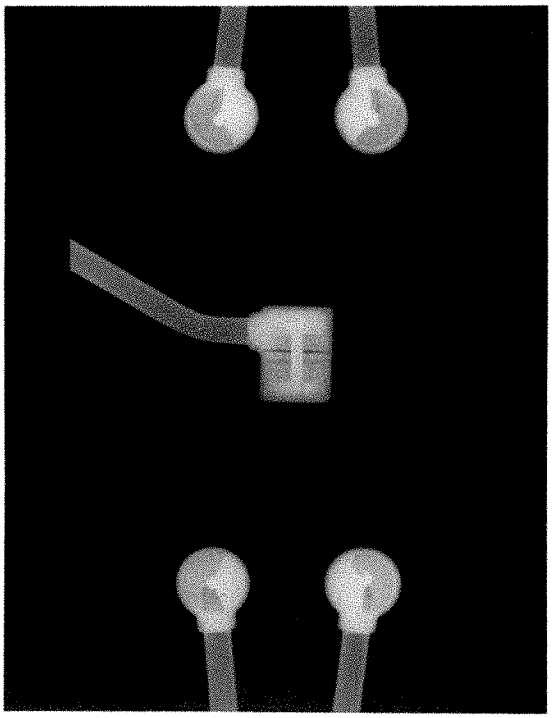


Fig. 3. Roentgenogram of ovoids showing source in exact center of source holder. Note radiodensity cast by tungsten blocks on medial aspect of superior-inferior surfaces of source holder.

Table I

RADIATION MEASUREMENTS COMPARING GREEN AND FLETCHER OVOIDS

A. Scintillation Probe (NaI [Tl] crystal) with analyzer-scaler, composition wood phantom, 25 μg. radium source, multiple exposure.

(1) Exposures perpendicular to source, average of 7 radians (45° angles) in planes

Plane	Radius	Green Ovoid	Fletcher Ovoid
	(cm.)	(mr/hr.)	(mr/hr.)
Upper ⅓	4.0	4.75	4.63
	5.75	3.27	3.17
	7.5	2.73	2.34
Middle ⅓	4.0	9.41	9.36
	5.75	4.62	4.58
	7.5	2.74	2.94
Lower ⅓	4.0	9.61	8.46
	5.75	4.22	3.94
	7.5	2.41	2.48

(2) Superior/inferior exposure

	Distance from Surface (cm.)	Green Ovoid (mr/hr.)	Fletcher Ovoid (mr/hr.)
Superior	2	6.7	5.9
	4	2.6	2.65
	6	1.6	1.65
	8	0.95	0.9
Inferior	2	8.6	9.1
	4	3.5	3.25
	6	1.95	1.8
	8	1.2	1.1

B. Lithium fluoride microrods, 22 mg. Ra Eq cesium 137 source, direct readings, composition wood and paraffin phantom

(1) Midplane exposure perpendicular to source

Distance from Surface (cm.)	Green Ovoid (rads/hr.)	Fletcher Ovoid (rads/hr.)
0	129.0	119.0
2	18.5	16.4
4	7.20	6.68
6	3.73	3.41
8	2.18	2.17
10	1.57	1.53
12	1.19	1.26

(2) Superior/inferior exposure

	Distance from Surface (cm.)	Green Ovoid (rads/hr.)	Fletcher Ovoid (rads/hr.)
Superior	0	61.70	53.20
	2	10.30	8.92
	4	5.66	5.17
	6	2.37	2.44
	8	1.50	1.67
	10	1.18	1.08
Inferior	0	59.43	55.60
	2	10.15	9.68
	4	5.92	5.85
	6	2.15	2.23
	8	1.56	1.62
	10	1.02	1.08



Fig. 2. Line drawing of afterloading vaginal ovoids to illustrate procedure of loading radioactive source.

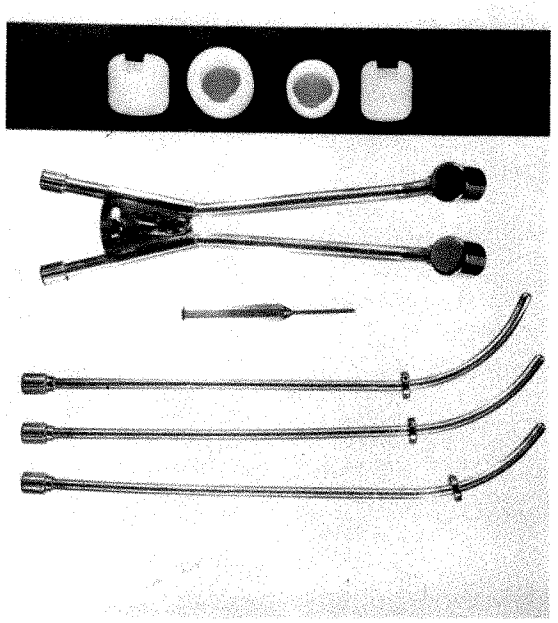


Fig. 4. Instruments taken to operating suite for insertion in typical case—afterloading ovoids and tandems, teflon sleeves, screwdriver for adjusting tandem collar.

for loading of radium sources—1 for the uterine tandem and 1 each for the vaginal ovoids.

Figure 4 shows the typical set of instruments taken to the operating suite for insertion. All can be cold sterilized in antiseptics or can be autoclaved.

The principal advantage of the afterloading system is the marked reduction in radiation exposure of personnel involved in radium therapy—radiotherapist, surgeon, anesthesiologist, nurses, recovery room workers, radiological technologists, transportation aides, etc. A survey of personnel film badge dosimeters over a 1 year period in a busy radiotherapy department shows only an occasional reading above 100 mrem per month. In the days before the afterloading technique, it was not uncommon for the radiotherapist and other personnel to receive an exposure dose of 25–40 mrem per radium case. A second advantage of afterloading is the ease of insertion and placement of applicators. Time can be taken to assure perfect positioning of the applicators and attention to detail in the vaginal packing. It is unusual to obtain less than a perfect roentgenographic position of the system (Fig. 5, *A* and *B*). Physician-trainees

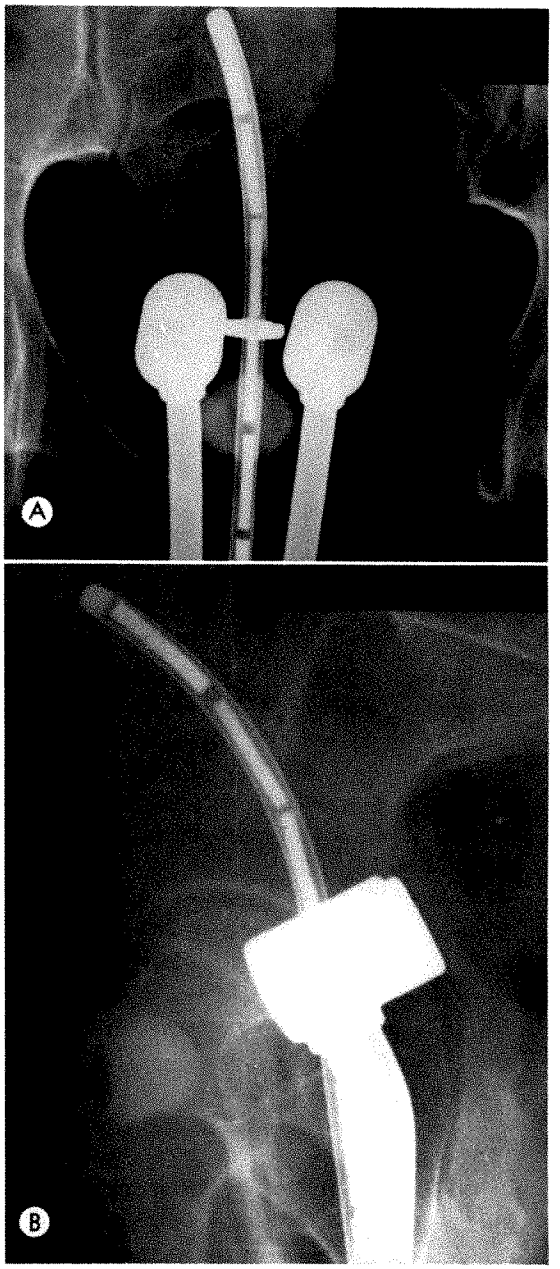


Fig. 5. (*A* and *B*) Anteroposterior and lateral roentgenograms of pelvis showing perfect position of uterine tandem and vaginal ovoids for treatment of carcinoma of the cervix uteri.

in radiotherapy or gynecologic surgery can be more adequately instructed in the techniques of applicator insertion and packing. The afterloading system can be inserted at the time of biopsy or curettage under anesthesia; the radium sources loaded after pathologic confirmation of the presence of neoplasm. The system can be loaded after dosimetry planning is completed. Finally, the time of radium application and removal can be adjusted to fit busy schedules more properly—gone should be the dinner hour or 3 A.M. radium applicator removals!

SUMMARY

An afterloading modification of the Fletcher vaginal ovoids for gynecologic radium therapy is described and illustrated. The afterloading ovoids have proven to be of great value in over 500 patient applications during the past 4 years. The many advantages of use of the afterloading system are stressed.

Allan E. Green, Jr., M.D.
Department of Radiology
Baptist Memorial Hospital
899 Madison Avenue
Memphis, Tennessee 38103

We acknowledge the aid of Messrs. William and Roy Sparkman in design and construction of the ovoids; J. W. Kersey, M.S. in radiation dosimetry studies; Messrs. Terry Kirk and Ronald Coleman for the illustrations; Mrs. Dianne Hayse for preparation of the manuscript; Luis Delclos, M.D., Odis Skinner, M.D., James Daly, M.D., and Robert R. Hughes, M.D. for valuable suggestions and aid in the clinical work.

REFERENCES

1. Fletcher, G. H., Shalek, R. J., Wall, J. A., and Bloedorn, F. G. Physical approach to design of applicators in radium therapy of cancer of cervix uteri. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1952, *68*, 935–949.
2. Fletcher, G. H., Wall, J. A., Bloedorn, F. G., Shalek, R. J., and Wooton, P. Direct measurements and isodose calculations in radium therapy of carcinoma of cervix. *Radiology*, 1953, *61*, 885–902.
3. Fletcher, G. H., Stovall, M., and Sampiere, V. Radiotherapy of cancers of cervix uteri. In: Carcinoma of the Uterine Cervix, Endometrium, and Ovary. Fifth Annual Clinical Conference on Cancer, University of Texas M. D. Anderson Hospital and Tumor Institute. Year Book Medical Publishers, Inc., Chicago, 1962.
4. Henschke, U. K. "Afterloading" applicator for radiation therapy of carcinoma of uterus. *Radiology*, 1960, *74*, 834–839.
5. Suit, H. D., Moore, E. B., Fletcher, G. H., and Worsnop, R. Modification of Fletcher ovoid system for afterloading, using standard-sized radium tubes (milligram and microgram). *Radiology*, 1963, *81*, 126–131.

THE ROLE OF PREOPERATIVE IRRADIATION IN THE TREATMENT OF CARCINOMA OF THE OVARY*

By JEROME M. VAETH† *and* FRANZ J. BUSCHKE‡
SAN FRANCISCO, CALIFORNIA

MALIGNANT ovarian tumors of müllerian origin are responsive to ionizing radiations. Both the number of long-term survivors and the length of survival are favorably influenced by the addition of radiation therapy to surgery and its management.[8] Why then are there not more survivors of this disease? Despite an emphasis on frequent routine pelvic examinations, this obviously is not the solution. The symptoms and signs are often innocuous enough that, when the disease is first diagnosed, it is frequently already in its advanced stages.

The minority of cases is surgically curable.[4] The concept of removing as much of the disease as possible, even if complete removal is obviously not possible, and following this surgical exercise by postoperative irradiation has not proved itself. Biologically, the approach by radical surgery plus postoperative irradiation is illogical, and survival figures bear this out. We are advocating a reappraisal of the roles of surgery and radiation therapy (and chemotherapy when indicated) in relation to each other. Rather than the administration of radiation therapy after an incomplete, potentially cancer-spreading type of surgical procedure, preoperative or, more accurately, preresection irradiation is indicated in the majority of cases of carcinoma of the ovary. Preoperative irradiation is indicated in Stage II and Stage III disease. Spread of tumor at the time of radical surgery is minimized if surgery is preceded by radiation therapy. The radiation response of the tumor is not jeopardized by surgical alteration of the tumor bed when preoperative irradiation is used. The response of the tumor to irradiation can be more accurately appraised if the tumor is left relatively undisturbed. The patient tolerates radical radiation therapy better if it is administered prior to radical surgery rather than after.

Lenz,[9] in a recent review of the experience at the Radiumhemmet, has advocated the use of preoperative irradiation in other than Stage I and Stage IV disease. Kottmeier,[8] in an earlier publication, has pointed out the futility of inadequate surgery in the management of this disease.

Preoperative irradiation has been reported in the past as having a role in the management of carcinoma of the ovary, but the cases reported are few.[7,11] Parks,[13] in 1945, reported 3 long-term survivors of advanced disease treated by medium voltage radiation therapy followed by resection. Long, Johnson and Sala[10] in 1967, in a review of 253 cases, reported 8 out of 8 eight year survivors in a group of Stage III patients irradiated prior to surgical resection of the tumor and pelvic organs. Bloedorn[3] stresses the role of preoperative irradiation based on his study of 163 cases of carcinoma of the ovary at the University of Maryland.

MATERIAL AND METHOD

The records of 30 successive patients with carcinoma of the ovary, personally treated by the authors at the University of California Medical Center from 1957 to 1963, were reviewed. These cases were staged according to the criteria suggested by the Cancer Committee of the International Federation of Gynecology and Obstetrics in 1964, as follows:

* Presented at the Fiftieth Annual Meeting of the American Radium Society, Miami Beach, Florida, April 7–11, 1968.
From the Department of Radiology, University of California Medical School, San Francisco, California.
† Associate Clinical Professor of Radiology, University of California Medical School, and Director, Claire Zellerbach Saroni Tumor Institute of San Francisco, Mount Zion Hospital and Medical Center.
‡ Professor of Radiology, University of California Medical School, and Chief, Section of Therapeutic Radiology, University of California Medical School, San Francisco, California.

Stage I. Growth limited to the ovaries
Stage Ia. Growth limited to one ovary
Stage Ib. Growth limited to both ovaries
Stage II. Growth involving one or both ovaries with pelvic extension
Stage IIa. Extension and/or metastasis to the uterus and/or tubes only
Stage IIb. Extension to other pelvic tissues
Stage III. Growth involving one or both ovaries with widespread intraperitoneal metastases to the upper half of the abdomen (the omentum, the small intestine and its mesentery)
Stage IV. Growth involving one or both ovaries with distant metastases outside the peritoneal cavity
Special Category. Unexplored cases which are thought to be ovarian carcinoma (surgery, explorative, or therapeutic, not having been performed)
Note. The presence of ascites should not influence the staging.

Two of the patients had been operated and irradiated prior to admission to the radiation therapy division, and 5 of the 30 patients were treated for distant metastases (Stage IV). These 7 cases were excluded from this study. There were 10 Stage II patients and 13 Stage III cases.

There was bilateral ovarian involvement in 22 of the 23 patients. The omentum was involved in 9 of 23 patients. Pelvic and/or periaortic lymph node metastases were not described in 9 of the 23 cases, but were found to be present in 4, and not present in 10 cases. The presence of lymph node involvement in operated cases varies considerably from the frequency reported by Bergman in autopsy cases (67 of 86 cases).[1] Only 2 patients had ruptured cysts or operative spillage; these 2 patients, however, did not receive chemotherapy. Ascites was present in 6 of the 23 patients and these patients received operative or immediate postoperative chemotherapeutic agents.

All patients were treated by supervoltage techniques—1 mev. roentgen therapy or Cobalt 60 teletherapy to the pelvis. Seventeen of the 23 patients received midpelvic doses above 5,000 rads in 6 to 7 weeks. The remaining 6 cases were treated to dose levels above 3,500 rads in approximately 4 weeks. Two cases were treated to the whole abdomen as well as the pelvis.

RESULTS

Of the 23 patients, 9 had excellent radiation response, as evidenced by regression and increased mobility of tumor masses. Five had no response. In 9, we were unable to evaluate the radiation response because there were no palpable masses postoperatively.

There were but 3 five year survivors without disease of the 23 patients: 1 Stage II patient of 10, and 2 Stage III patients of 13.

Twenty of the patients were treated in the "classic" fashion, that is, removal of the uterus, fallopian tubes, ovaries, and "as much tumor as possible," followed by postoperative irradiation with chemotherapy utilized when indicated. There were 2 survivors free of disease in this group. Three cases were not subjected to the "routine" surgery and postoperative irradiation scheme. Two were treated after exploratory laparotomy by radiation therapy only; none survived. One patient was treated after exploration and biopsy by radiation therapy, followed by bilateral salpingo-oophorectomy and hysterectomy with tumor removal. This patient is a $7\frac{1}{2}$ year survivor, free of disease. There are 2 patients alive 5 years, but with disease. These 2 patients have been excellently maintained on judicious chemotherapy.

Two of the 3 cases mentioned appear illustrative of the authors' sentiments; that is, (1) preoperative irradiation is efficacious in properly selected cases; and (2) despite satisfactory radioresponse and disappearance of palpable tumor following radiation therapy, the patient with cancer of the ovary should be surgically re-explored after irradiation.

REPORT OF CASES

Preoperative Irradiation and Long-term Survival

Case 1. E. P., a 32 year old woman, had a 6

week history of "fullness" of the abdomen. A laparotomy revealed bloody ascites and a mass filling the pelvis which was adherent to the pelvic side-walls and the bowel, and was invading the uterus and fallopian tubes. There were pelvic and abdominal peritoneal implants noted. A biopsy of the pelvic mass revealed papillary serous cystadenocarcinoma of the ovaries. No further surgery was performed. The patient received whole pelvis irradiation on the cobalt 60 teletherapy unit, 5,600 r, mid-pelvis, delivered in 51 days. There was excellent regression of the pelvic and abdominal masses during radiation therapy. At re-exploration, approximately 6 weeks later, tumor masses were noted in the pelvis but these were no longer adherent to the pelvic side-walls and pelvic structures, and were easily delivered with knife dissection. A bilateral salpingo-oophorectomy and a hysterectomy were performed. There was an uneventful postoperative recovery without healing difficulty. The patient is alive and free of disease 7½ years after radiation therapy and surgical resection.

Comment. This case illustrates the proper relationship of surgery and radiation therapy to each other in Stage II and Stage III carcinoma of the ovary. Although there was not complete disappearance of the pelvic masses, there was good radiation response and the patient was given the benefit of a surgical re-exploration. At this time, complete tumor removal was possible as well as removal of the pelvic organs, resulting in long-term survival free of disease.

Opportunity Lost.

CASE II. M. R., a 53 year old woman, detected an enlarging abdomen over approximately 2 months. A pelvic mass was palpated which was bilateral and movable. At laparotomy, both ovaries were found to be cystic and massively involved with tumor. A cyst was inadvertently ruptured. The tumor was found to be invading the adjacent omentum and there were pelvic peritoneal implants. The diagnosis was papillary cystadenocarcinoma. The omentum was removed; Thio-Tepa was instilled in the abdominal and pelvic cavities. Cobalt 60 teletherapy was administered to the pelvis and lower abdomen to a mid pelvic dose of 5,000 r in 47 days. The palpable tumor disappeared under radiation therapy. The patient was well and free of disease for 3 years and 10 months until she again noted an enlarging abdomen and pelvic pain. The tumor was found to have recurred in the pelvis. She developed supraclavicular lymph node metastases, ascites, and liver metastases. She died 2 months later.

Comment. This patient was a victim of misguided medical optimism. Re-exploration following irradiation was indicated in this patient despite the disappearance of tumor.

SUMMARY

A re-evaluation of the role of preoperative irradiation is indicated in the management of carcinoma of the ovary. The patient should be accurately staged and this can only be achieved by laparotomy. At this time, a biopsy is performed.

For Stage I, surgical extirpation of the tumor and removal of the pelvic organs is adequate treatment. Chemotherapy is administered if there is operative spill or ascites.

In Stage II, no further surgery is performed initially other than biopsy. Chemotherapy, both intracavitary and systemic, may be administered if there is ascites and/or operative spill. The patient should then be given radical radiation therapy of supervoltage or megavoltage quality. In our experience, doses of 5,000–5,500 r to the pelvis are well tolerated at a rate of slightly less than 1,000 r per week in 4 to 5 fractions weekly, and are sufficient for preoperative purposes.

In Stage III, the management is similar to that in Stage II. Abdominal implants have been at times controlled by treatment to the pelvis only. If treatment to the upper abdomen is elected, lower dose levels than that administered to the pelvis are in order. Doses above 3,000 r are poorly tolerated and morbidity is increased.

In Stages II and III, the patient should be examined carefully during and following radiation therapy to ascertain when the maximum regression of the tumor has occurred, and re-exploration should not be performed any earlier than 4 weeks after

the completion of radiation therapy. Even if there is total disappearance of tumor, the patient should be re-explored. A thorough diagnostic study should be performed before re-exploration. The patient should have a chest roentgenogram and if this is suspect, a tomographic study of the chest. Blood chemistries and a liver scan should be performed in an effort to rule out the presence of metastases. If these studies are not indicative of metastases, the patient is submitted to surgery. At the time of surgery, complete removal of the tumor should be performed along with complete removal of the pelvic organs.

In Stage IV disease, surgery should be limited only to achieve palliation. Likewise, radiation therapy is indicated only if there is a possibility of providing palliation. Chemotherapy may add to long-term and comfortable survival for many of these patients.[2,4,15]

Dr. James A. Corscaden has stated, "Certainly the partial removal of ovarian carcinoma, and subsequent irradiation, has not given very satisfactory results. The other procedure (that is, preoperative irradiation) would at least be worth trying."[13]

Jerome M. Vaeth, M.D.
Claire Zellerbach
Saroni Tumor Institute of San Francisco
Mount Zion Hospital and Medical Center
1600 Divisadero Street
San Francisco, California 94115

REFERENCES

1. Bergman, F. Carcinoma of ovary: clinicopathological study of 86 autopsied cases with special references to mode of spread. *Acta obst. et gynec. scandinav.*, 1966, *45*, 211–231.
2. Blinick, G., Kabakow, B., Wallach, R. C., and Antopol, W. Treatment of advanced inoperable ovarian carcinoma with thio-tepa. *Am. J. Obst. & Gynec.*, 1966, *96*, 425–429.
3. Bloedorn, F. Personal communication.
4. Burns, B. C., Jr., Rutledge, F. N., Smith, J. P., and Delclos, L. Management of ovarian carcinoma: surgery, irradiation, and chemotherapy. *Am. J. Obst. & Gynec.*, 1967, *98*, 374–386.
5. Copenhaver, E. H., and Abu-Rustum, S. Management of primary carcinoma of the ovary. *S. Clin. North America*, 1967, *47*, 715–722.
6. Gilbertson, V. A., and Wangensteen, O. H. Summary of thirteen years experience with second look program. *Surg., Gynec. & Obst.*, 1962, *114*, 438–442.
7. Harris, J. H., and Payne, F. L. Value of irradiation in treatment of ovarian carcinoma. *Am. J. Obst. & Gynec.*, 1935, *29*, 88–93.
8. Kottmeier, H. L. Radiotherapy in treatment of ovarian carcinoma. *Clin. Obst. & Gynec.*, 1961, *4*, 865–874.
9. Lenz, M. Seropapillary and endometrioid carcinoma of ovary; survival rate after surgery and radiotherapy. UICC Monograph Series. Volume II. Ovarian Cancer.
10. Long, R. T. L., Johnson, R. E., and Sala, J. M. Variations in survival among patients with carcinoma of ovary: analysis of 253 cases according to histologic type, anatomical stage and method of treatment. *Cancer*, 1967, *20*, 1195–1202.
11. Marchetti, A. A. Ovarian cancer: clinicopathologic evaluation. *New York J. Med.*, 1941, *41*, 2324–2331.
12. Maus, J. H., Mackay, E. N., and Sellers, A. H. Cancer of ovary: twenty-one year study of 1,722 patients treated in Ontario Cancer Clinics, 1938–1958 inclusive. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1968, *102*, 603–607.
13. Parks, T. J. Carcinoma of ovary treated preoperatively with deep x-ray: report of three cases. *Am. J. Obst. & Gynec.*, 1945, *49*, 676–685.
14. Sagerman, R. H., Hanks, G. E., and Bagshaw, M. A. Supervoltage radiation therapy: use of linear accelerator for treating ovarian adenocarcinoma. *California Med.*, 1965, *102*, 118–122.
15. Schwartz, E. E., Sklaroff, D. M., and Levick, S. N. Value of chemotherapy in irradiation of ovarian carcinoma. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1966, *96*, 158–165.

THE CLINICAL COURSE OF HODGKIN'S DISEASE AND OTHER MALIGNANT LYMPHOMAS TREATED WITH RADICAL RADIATION THERAPY*

By LEONARD R. PROSNITZ, M.D.,† SAMUEL HELLMAN, M.D.,‡ CARL F. VON ESSEN, M.D., *and* MORTON M. KLIGERMAN, M.D.
NEW HAVEN, CONNECTICUT

HODGKIN'S disease in recent years has increasingly come to be viewed as a disorder which begins in a local focus, spreads to adjacent lymph node bearing areas and is potentially curable with high-dose radiation therapy. Evidence for this view has been presented by Easson,[2] Peters,[11] and Kaplan.[8] Easson states that malignant lymphomas other than Hodgkin's disease behave in a similar fashion and may also be curable with appropriate radiation therapy.

A number of questions, however, have not been fully answered, among them the following: What is the fate of patients treated with radical radiation therapy, not only in terms of their survival, but also how does reactivation of the disease manifest itself? Is "prophylactic" treatment to adjacent lymph node areas beneficial? What is the proportion of patients with lymphomas who have localized disease and thus fall into a potentially curable group? Does the population seen by a Radiation Therapy Department differ significantly from the over-all group with the disease? What are the differences, if any, in the behavior of the lymphomas other than Hodgkin's disease? This study was undertaken in an attempt to clarify some of the above points.

MATERIAL AND METHODS

The records of all 278 patients with malignant lymphomas seen in the Department of Radiation Therapy of Yale-New Haven Hospital during the years 1958–1966 were analyzed. All patients had a diagnosis confirmed histologically by the Pathology Department of this hospital. All patients were restaged according to the classification proposed by the conference on Hodgkin's disease at Rye, New York in September 1965 (Table 1).[13] Staging was largely done without the help of lymphangiograms, bone marrow biopsy and liver biopsy, these procedures coming into use only in the last few years of the study.

TABLE I

STAGING OF LYMPHOMAS

Stage I.	Disease limited to 1 anatomic region or to 2 contiguous anatomic regions on the same side of the diaphragm
Stage II.	Disease in more than 2 anatomic regions or in 2 noncontiguous anatomic regions on the same side of the diaphragm
Stage III.	Disease on both sides of the diaphragm but not extending beyond the involvement of lymph nodes, spleen and/or Waldeyer's ring
Stage IV.	Involvement of the bone marrow, lung parenchyma, pleura, liver, bone, skin, kidneys, gastrointestinal tract or any tissue or organ in addition to lymph nodes, spleen or Waldeyer's ring

A and B subclasses indicate absence or presence of systemic symptoms respectively. The following documented symptoms are significant: (a) fever; (b) night sweats: (c) pruritus.

Radical treatment, defined as a minimum of 3,000 rads to all areas of known disease

* Presented at the Fiftieth Annual Meeting of the American Radium Society, Miami Beach, Florida, April 7–11, 1968.
From the Department of Radiology, Yale University School of Medicine and the Radiological Service of the Yale-New Haven Hospital, New Haven, Connecticut.
Supported in part by USPHS Grant, CA-06519 and TI CA -5094 of the National Cancer Institute.
† Fellow in Radiation Therapy supported by the National Cancer Institute Training Grant CA-05094.
‡ Present Address: Department of Radiology, Harvard University School of Medicine, Boston, Massachusetts.

with intent to cure, was given to most Stage I and II patients. The median tumor dose was actually 3,600 rads with 90 per cent of patients treated radically receiving 3,500 rads or more. Radical radiation therapy to patients presenting with Stage III disease was begun only toward the end of 1966 and no such patients are included in this study. Treatments were carried out principally on a 2 mev. Van de Graaff generator during the years 1958–1962 and on a 6 mev. Linear Accelerator from 1963–1966. Opposing fields were generally used and doses were calculated on the basis of the minimum tumor dose. The dose rate was 800–1,000 rads per week. "Local" therapy consisted of treatment to the area grossly involved by tumor with a variable margin of normal tissue. "Extended field" treatment consisted essentially of the "mantle" technique described by Kaplan[8] in which the neck, axillae and mediastinum to the level of the diaphragm were irradiated in continuity.

Survival calculations were done for those patients in whom a course of planned radical radiation therapy was begun. In the early years of the study, some Stage I and II patients were not treated radically and the survival of these patients is also included. Patients in Stages I–IV treated both radically and palliatively were considered in the calculation of recurrence rates. Patients were followed from a minimum of 1 year to a maximum of 10 years. No patients with Hodgkin's disease were lost to follow-up. Survival curves and recurrence rates were calculated using the method of Berkson and Gage[1] without correcting for age.

RESULTS

The total number of patients with Hodgkin's disease seen by the Radiation Therapy Department in the years 1958–1966 was 142. Their breakdown by stage is given in Table II. Of the cases recorded by the Tumor Registry of Yale-New Haven Hospital during the same 9 year period, 24 had not been sent for radiation therapy consultation. Thus, over 80 per cent of all patients with Hodgkin's disease at this hospital were seen in the Radiation Therapy Department. Similarly, 44 patients with lymphosarcoma, reticulum cell sarcoma and follicular lymphoma were listed with the Tumor Registry who had not been evaluated by the Radiation Therapy Department. Thus, those seen by the Radiation Therapy Department represent 68 per cent of the total.

TABLE II

PATIENTS WITH MALIGNANT LYMPHOMA SEEN IN THE RADIATION THERAPY DEPARTMENT

	Hodgkin's Disease	Other Lymphomas
Stages I and II	79	36
radical therapy	54	20
Stages III and IV	51	50
Unclassified	12*	50†
Total (lines 1, 3, and 4)	142	136

* Information incomplete for staging.

† Lymphomas originating outside the lymphatic system (25 cases) and those with information incomplete for staging (25 cases).

HODGKIN'S DISEASE

Staging. Those patients with Hodgkin's disease treated with radical radiation therapy, their stage and their outcome are shown in Table III. Thirty-seven of the 54 patients are currently living and well without evidence of disease. Patients with systemic symptoms (Stage IB and IIB) fared

TABLE III

HODGKIN'S DISEASE—TREATED WITH 3,000 RADS OR MORE

Stage		Living Free of Disease	Living with Disease	Dead	Total
I	A	25	5	6	36
	B	1	2	1	4
II	A	9	3		12
	B	2			2
		37	10	7	54

TABLE IV

HODGKIN'S DISEASE—DISTRIBUTION BY SEX

Stage		Living Free of Disease		Living with Disease		Dead		Total	
		M	F	M	F	M	F	M	F
I	A	12	13	3	2	4	2	19	17
	B		1	2		1		3	1
II	A	2	8	2				4	8
	B	1	1					1	1
		15	23	7	2	5	2	27	27

somewhat worse, only 3 of 6 being living and free of disease. Stage II patients did somewhat better than Stage I cases, 11 of 14 surviving without disease as opposed to 26 of 40 Stage I cases.

The distribution of cases by sex is shown in Table IV. The survival in women is superior to that in men, 23 of 27 now living and being free of disease compared to 15 of 27 men. The preponderance of women in Stage II may have influenced the improved survival rate in this stage.

The age of the patients, divided into 3 groupings, is given in Table V. In this series, stage for stage, the age of the patient appeared to make little difference in the outcome.

Survival. Cumulative survival curves for radically treated Stage I and II patients with Hodgkin's disease are shown in Figure 1. The upper curve represents all living patients. The lower curve considers only those living and free of disease as alive, those living with disease being eliminated at the time of the first reactivation. The cumulative survival rates for the 2 groups are 82 per cent and 55 per cent, respectively, at 5 years. Survival in Stage I and II patients not treated radically is shown in Figure 2. Thirty-five per cent survived 5 years, but no survivor at 5 years was free of disease.

Lymphangiography was performed on 21

TABLE V

HODGKIN'S DISEASE
DISTRIBUTION BY AGE, STAGE, AND OUTCOME

Stage		Living, Free of Disease			Living with Disease		
		0–20	20–50	50+*	0–20	20–50	50+
I	A	8	14	3	3	1	1
	B	1			1	1	
II	A	4	5		2	1	
	B		2				
		13	21	3	6	3	1

Stage		Dead			Total		
		0–20	20–50	50+	0–20	20–50	50+
I	A	1	4	1	12	19	5
	B		1		2	2	
II	A				6	6	
	B					2	
		1	5	1	20	29	5

* The 0–20, 20–50, 50+ refer to age of the patient in years.

patients with Hodgkin's disease during the course of the study. Three were interpreted as positive for intra-abdominal disease, thus placing the patients in Stage III. They did not receive radical radiation therapy. Thirteen of the 18 patients with normal lymphangiograms are living and free of disease compared with 24 of 36 living without disease staged without benefit of lymphangiography.

Reactivation. The terms reactivation, recurrence, true recurrence, extension, and dissemination are being used increasingly to describe the events in the history of lymphomas and they will be so used in this paper. They are defined in Table VI.

Figure 3 presents the cumulative reactivation rate for the Hodgkin's disease patients who were radically treated. On constructing this curve, only the time of initial reactivation was considered. The reactivation rate rises sharply initially but then levels off after reaching a peak of 55 per cent after 4 years. No *initial* reactivations occurred in this series after this time.

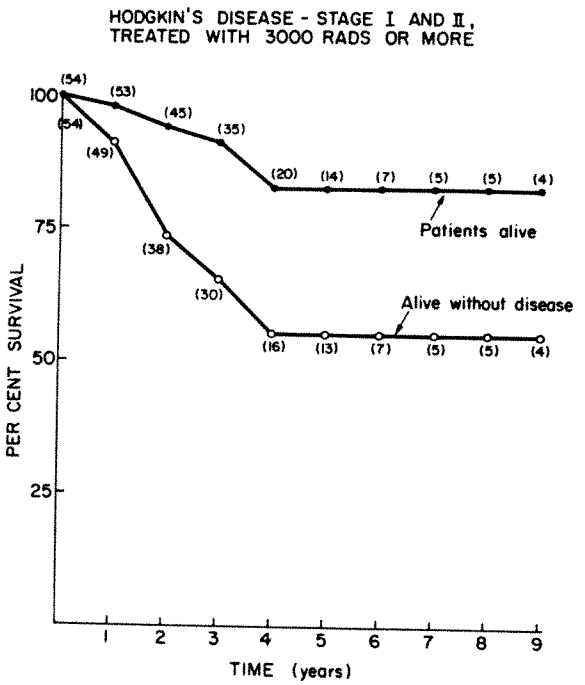


FIG. 1. Cumulative survival rates in patients with Stage I and II Hodgkin's disease treated with radical radiation therapy. The upper curve includes all patients. The lower one eliminates those living with disease at the time of the first reactivation. The numbers in parentheses represent the number of patients at risk.

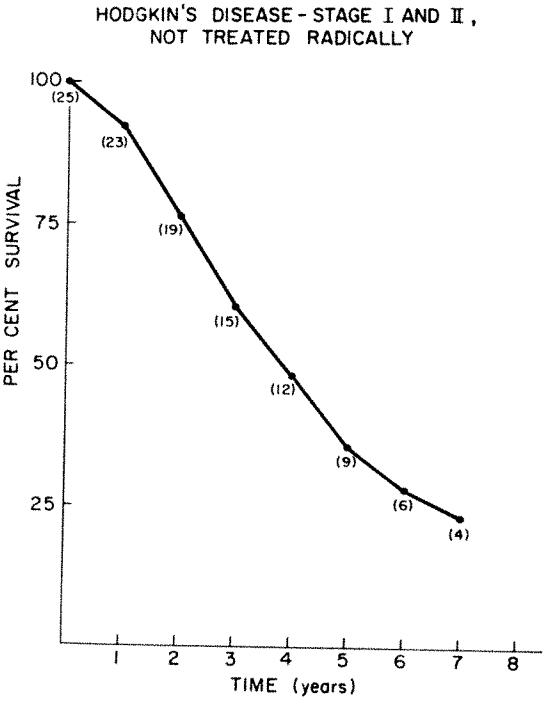


FIG. 2. Cumulative survival in Stage I and II patients with Hodgkin's disease *not* treated with radical radiation therapy.

The first reactivation event of the 54 patients with Hodgkin's disease treated radically is shown in Table VII. In no instance did a recurrence constitute the first sign of reactivation. Reactivation did not necessarily render a patient incurable. Of those patients presently alive and free of disease, 9 had a total of 16 extensions successfully treated.

TABLE VI

TYPES OF REACTIVATION

Reactivation: Any new sign of disease activity
Recurrence: New disease occurring within a previously treated area
True Recurrence: A recurrence as the first sign of reactivation
Extension: New disease outside a previously treated area but still confined to the lymphatic system
Dissemination: New disease outside of the lymphatic system

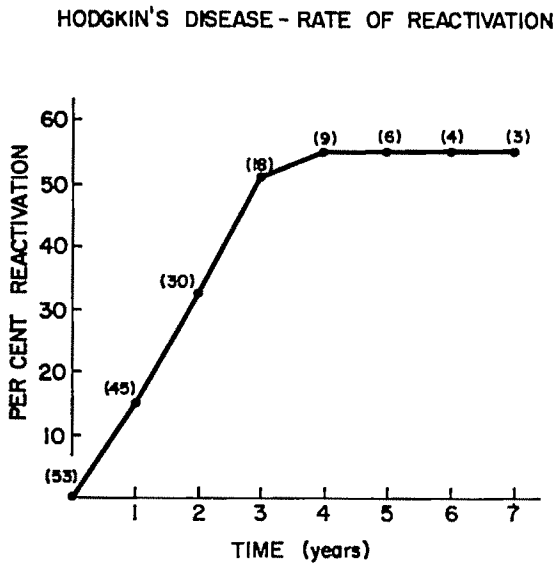


FIG. 3. Cumulative reactivation rate in patients with Stage I and II Hodgkin's disease treated with radical radiation therapy.

TABLE VII

FIRST REACTIVATION IN PATIENTS WITH HODGKIN'S DISEASE TREATED RADICALLY*

	Extension	Dissemination
Living Free of Disease (37 patients)	9†	—
Living with Disease (10 patients)	4‡	6
Dead (7 patients)§	3	3
	16	9

* No recurrences took place as the first reactivation event.
† 9 patients had 16 extensions.
‡ 4 patients had 6 extensions.
§ In 1 patient, type of initial reactivation unknown.

The sites of the extensions of disease in the 9 patients who are alive and well after treatment of their extensions with radiation and the relationship of the areas of extension to the original treatment portal are diagrammed in Figure 4. Figure 5 shows the areas of extension and original portal size in 7 patients who subsequently died or are living with disease. In both groups of extensions, there were four instances where the adjacent lymph node bearing area had not been grossly involved with disease initially but had been treated "prophylacti-

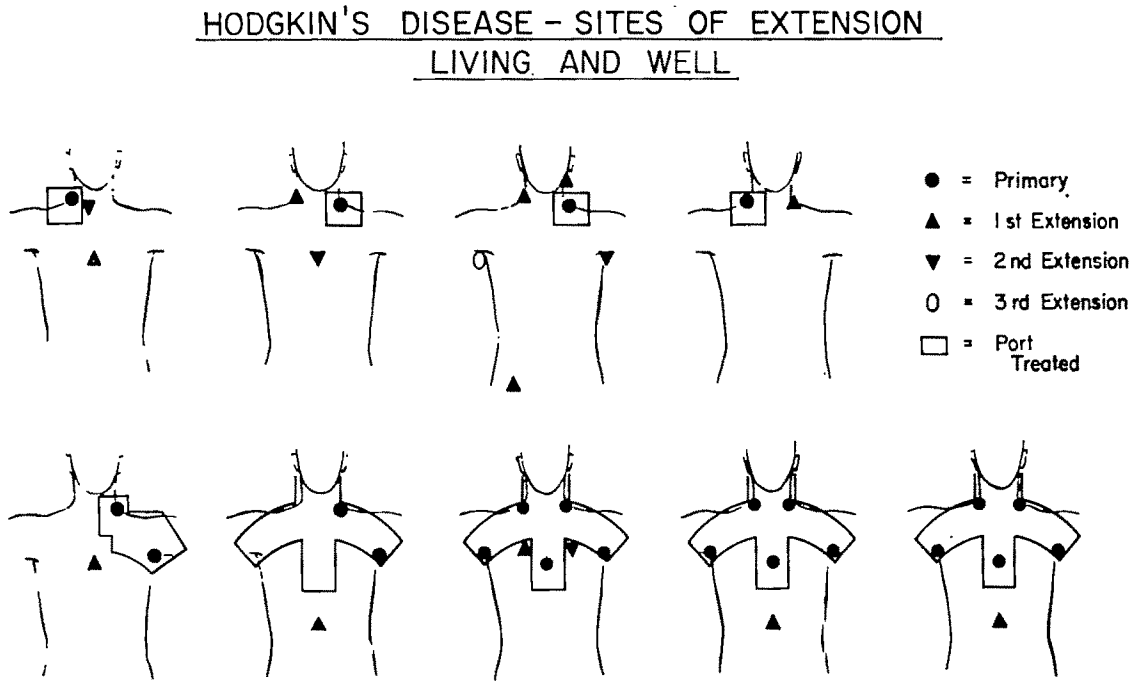


FIG. 4. The sites of extension and original portals in 9 patients with Stage I and II Hodgkin's disease who had been treated radically. The extensions were treated successfully with radiation therapy and the patients are currently living and free of disease.

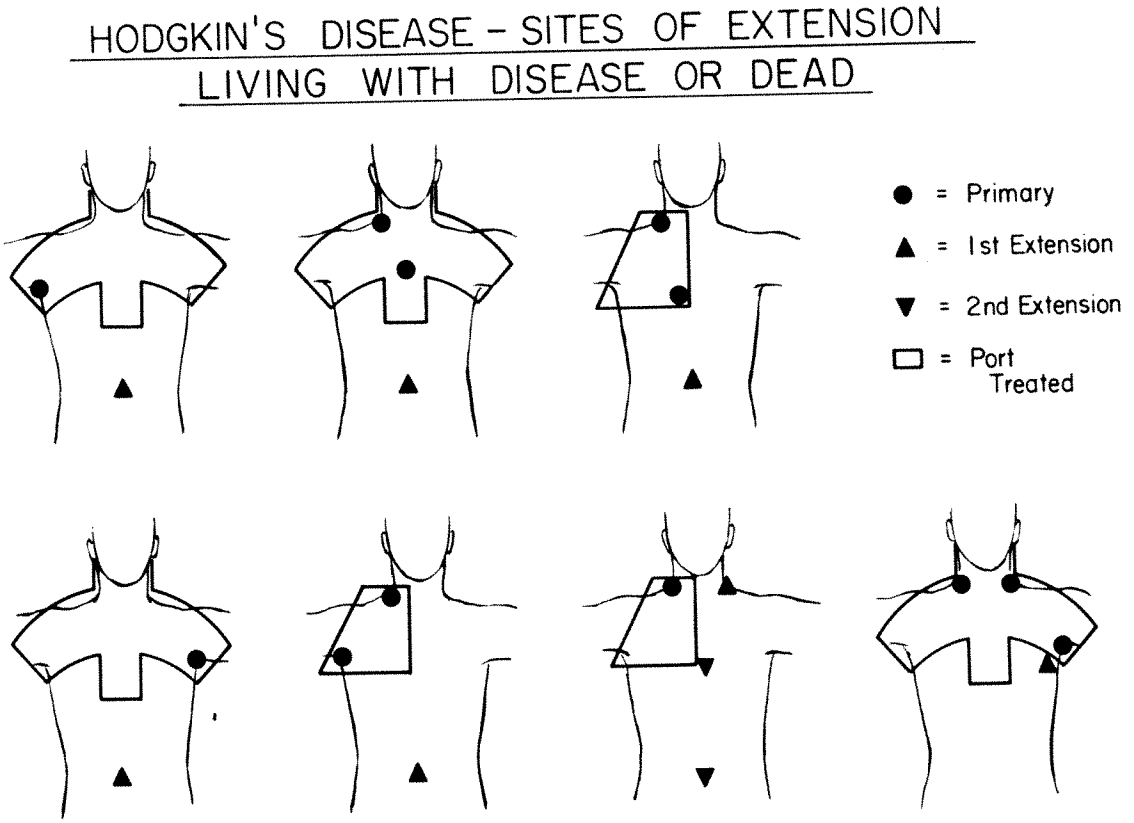


Fig. 5. The sites of extension and original portals in 7 Stage I and II patients with Hodgkin's disease who had been treated with radical radiation therapy who are currently either dead or alive with disease.

cally." All four instances involved the mediastinum as the clinically uninvolved area and the para-aortic region as the site of extension. The one inguinal extension skipped an area not involved with disease. A comparison of the sites of extension in patients who are living and well with those who are alive with disease or dead is found in Table VIII.

The relationship of survival to the use of local or extended field therapy is summarized in Table IX. Ten of 18 patients treated locally are living and free of disease as contrasted to 27 of 36 treated with an extended field. The number of extensions in patients treated locally was greater than in those receiving extended field therapy. Of the 18 patients treated locally, 8 had a total of 16 extensions. Eight of 36 patients treated with an extended field had 9 extensions.

As an index of local control of Hodgkin's disease, cumulative recurrence rates for fields treated with two different dose levels of radiation are plotted in Figures 6 and 7. Recurrences within the treated field in patients with Stages I–IV are described in Figure 6. Recurrence rates in patients who

Table VIII

SITES OF EXTENSION OF HODGKIN'S DISEASE TREATED RADICALLY

	Living and Well (9)	Living with Disease or Dead (7)
Cervical	5	1
Axillary	2	1
Infraclavicular	2	
Mediastinal	3	1
Para-aortic	3	6
Inguinal	1	
Total Extensions	16	9

TABLE IX

HODGKIN'S DISEASE—EXTENT OF TREATMENT AND SURVIVAL

Stage	Living Free of Disease		Living with Disease		Dead		Total	
	Extended Field	*Local*	*Extended Field*	*Local*	*Extended Field*	*Local*	*Extended Field*	*Local*
I A	16	9	2	3	3	3	21	15
B	1		2			1	3	1
II A	9		2	1			11	1
B	1	1					1	1
	27	10	6	4	3	4	36	18

were Stage I and II at the onset of their disease are given in Figure 7. No *true* recurrences were seen in any patient treated with more than 3,000 rads. In the Stage I and II patients treated with 2,000–3,000 rads, 3 *true* recurrences took place. In patients with both localized and generalized disease, recurrence rates were approximately twice as great in the group treated with 2,000–3,000 rads, compared with those receiving doses in excess of 3,000 rads.

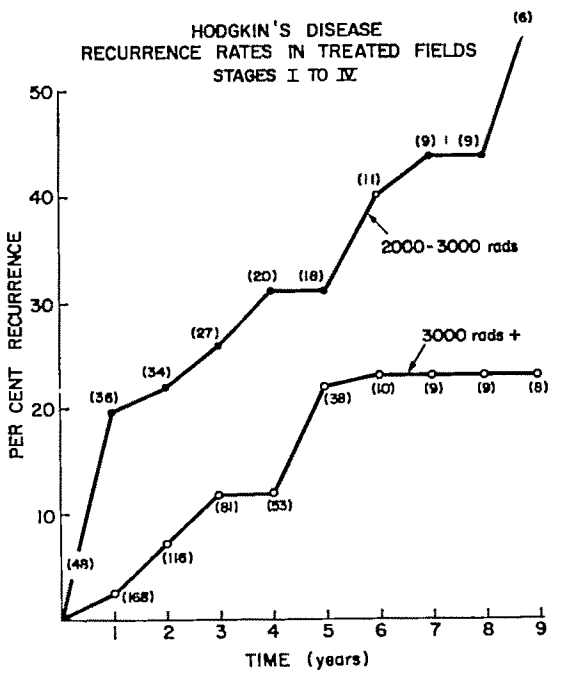


FIG. 6. Cumulative recurrence rates in patients in all stages of Hodgkin's disease treated with different dose ranges. The numbers in parentheses refer to the number of fields at risk.

LYMPHOMAS OTHER THAN HODGKIN'S DISEASE

In a consideration of malignant lymphomas other than Hodgkin's disease (lymphosarcoma, reticulum cell sarcoma, and fol-

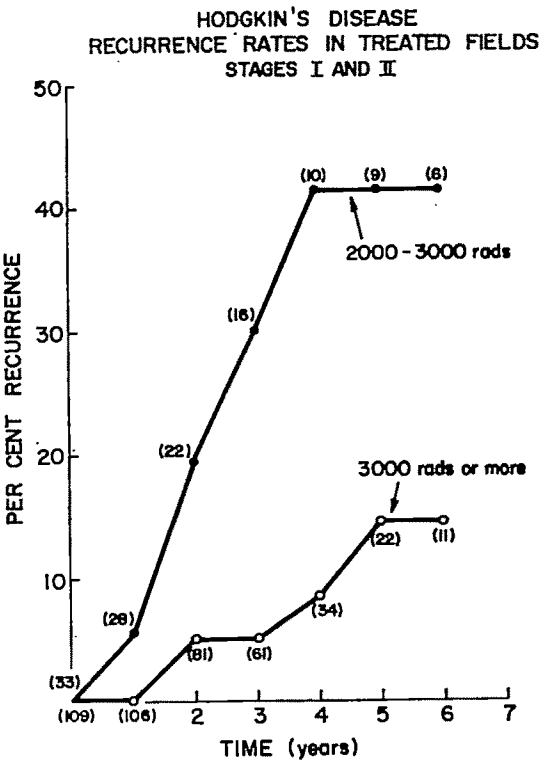


FIG. 7. Cumulative recurrence rates in patients with Stage I and II Hodgkin's disease treated with two different dose levels. Note the similarity between this and Figure 6 indicating that the differences between patients in early and late stages of disease are not responsible for the differences in recurrence rates observed with different dose levels of radiation.

licular lymphomas), a number of differences are apparent. Only 36 of 136 patients (22.4 per cent) presented with localized disease; *i.e.*, Stage I or II (Table II). Twenty of these received radical radiation therapy (a minimum of 3,000 rads to all areas of known disease). The results of treatment of these patients are shown in Table X. The outcome for Stage I patients was considerably better than that for Stage II, although the numbers are small. Seven of 12 Stage I patients survived free of disease for periods of 3 to 8 years. All Stage II patients died of disease. The Stage I group comprised 7 patients with lymphosarcoma, 3 patients with follicular lymphoma and 2 patients with reticulum cell sarcoma. Four of the 5 Stage I cases who died or are living with disease had lymphosarcoma and the fifth had follicular lymphoma. The Stage II patients consisted of 7 with lymphosarcoma and 1 with reticulum cell sarcoma.

Of the 7 surviving patients, 1 had an area of direct extension of disease that was successfully treated with radiation, the patient being free of disease at present. Of the 13 patients living with disease or dead, 8 had dissemination as their first sign of reactivation, 4 had an extension with a skipped area, and 1 had extension of an adjacent area. All initial instances of reactivation occurred within the first 3 years, 10 of them within the first year. All of the patients except one were treated locally with a generous margin. There was only one instance of the extended field type of therapy employed for Hodgkin's disease.

TABLE X

LYMPHOMAS OTHER THAN HODGKIN'S DISEASE TREATED WITH 3,000 RADS OR MORE

Stage	Living Free of Disease	Living with Disease	Dead of Disease	Total
I A	7*	2	3	12
II A	0	0	8	8
	7	2	11	20

* 2 patients died of myocardial infarctions 3 years and 8 years after treatment, respectively, with no evidence of disease.

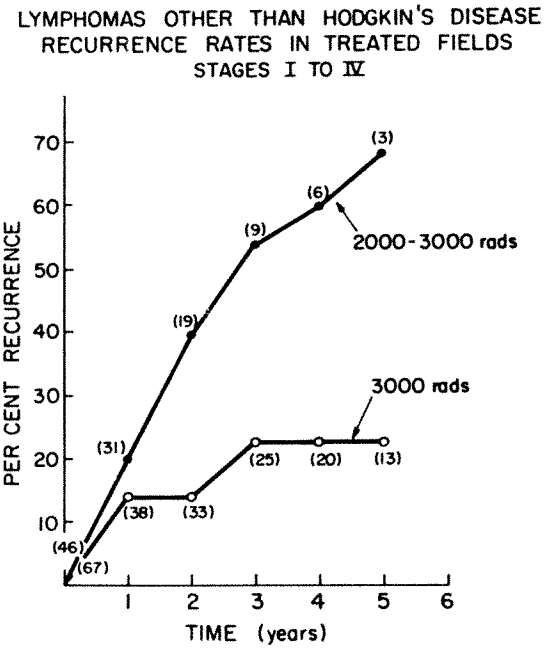


FIG. 8. Cumulative recurrence rates in patients in all stages of malignant lymphomas other than Hodgkin's disease treated with two different dose levels of radiation.

Eight patients with primary extranodal lymphoma of the head and neck area were treated with 3,500 rads or more in a radical fashion to all known disease. This group comprised 5 patients with reticulum cell sarcoma, 2 with lymphosarcoma and 1 with follicular lymphoma. Six of the 8 are living and free of disease at intervals of 2 to 9 years. Two patients, both of whom had reticulum cell sarcoma, died of disseminated disease within 6 months.

Cumulative recurrence rates for lymphosarcoma, reticulum cell sarcoma and follicular lymphoma treated with 2,000–3,000 rads and more than 3,000 rads are plotted in Figure 8. Again there was no instance of a *true* recurrence in the group receiving 3,000 rads. Those patients treated with lower doses had a steadily rising recurrence rate which reached 68 per cent after 5 years. Those receiving in excess of 3,000 rads had a maximum recurrence rate of 25 per cent which leveled off after 3 years, after which no recurrences were seen. These recurrence data are very similar to that of the patients with Hodgkin's disease. Because of the

small number of cases, further comparisons of recurrence rates at different doses in patients with different stages of disease could not be made.

COMPLICATIONS

No serious complications of treatment were seen in either the patients with Hodgkin's disease or those with other lymphomas. Six patients developed pulmonary fibrosis visible on chest roentgenography but are asymptomatic. Evidence of an effect on the spinal cord as manifested by development of a transient Lhermitte's sign was occasionally seen. Clinically significant bone marrow depression was infrequent even in the extended field group and was a problem chiefly in those patients who had abdominal extensions that were treated.

DISCUSSION

This report provides further evidence that radical radiation therapy of Stage I and II Hodgkin's disease results in a significant percentage of long-term survivors, exceeding that observed in patients who were not so treated in the past. In our series, the 5 year survival rate was 82 per cent including all living patients, and 55 per cent including only those patients alive and free of disease. In contrast, 35 per cent of Stage I and II patients not treated radically survived 5 years. However, none of these patients was alive and free of disease.

These results are comparable to those obtained by previous investigators in patients with Stage I and II disease similarly treated. Five year survival rates of 65 per cent, 55 per cent, 56 per cent, and 55 per cent have been reported by Peters,[11] Kaplan,[6] Easson,[2] and Fayos *et al.*,[3] respectively. Survival rates in patients who received low dose radiation therapy or no treatment in the past have ranged from approximately 25 to 37 per cent at 5 years.[3,7,9,16] Because no group (including ours) reporting results of therapy has randomized its cases between low dose and radical treatment, no strict comparison of these results with survival in patients not treated radically is possible. It should be emphasized that many reports of survival data do not specify if the patients are free of disease as well as being alive. Undoubtedly many of them are not—a factor responsible for the fewer number of 10 year survivors than 5 year survivors.

If one accepts the concept of the curability of localized Hodgkin's disease, it is important to determine what percentage of patients have localized disease at the onset. In our series, 56 per cent of the patients were Stage I or II when examined initially. Comparison with the data for Yale-New Haven Hospital as a whole indicates that 80 per cent of all patients with Hodgkin's disease were seen in the Radiation Therapy Department. Thus, a minimum of 45 per cent of all hospital cases were Stage I and II, assuming that the 20 per cent not seen in this department were all Stage III and IV. In Rosenberg and Kaplan's series[14] the percentage of patients with Stage I and II disease was 57. Easson's figures are different, 35 per cent of patients with Hodgkin's disease having localized disease.[2] However, all Stage I and II patients would not be included in what he terms "localized disease."

The data on reactivation of Hodgkin's disease provide additional support for the concept of spread of the disease in a contiguous fashion. Sixteen patients had spread of the disease to the next lymph node bearing area outside the treatment field. In 12 of these 16, the extensions were adjacent to a site that had been grossly involved with disease. In the other 4 patients, the extensions were next to an area that had been treated "prophylactically" but had not been grossly involved. These 4 may or may not represent discontinuous extensions. One patient had an extension to an area that was not contiguous. Widespread dissemination as the initial sign of reactivation occurred in 9 patients. The high incidence of extension to adjacent areas is an argument for treating these areas "prophylactically" initially, especially when the treatment is above the diaphragm and can be given with relatively little increase in morbidity. Although a statistically significant survival difference

cannot be demonstrated for extended field therapy *versus* local therapy, because of the relatively small number of patients in each group, we feel that each extension is a threat to the patient's survival. Less of them occur with extended field therapy. Giving additional radiation therapy to contiguous extensions also creates the problem of matching multiple field edges.

The data on recurrence rates in treated fields indicate that local control of Hodgkin's disease is best achieved with doses greater than 3,000 rads. The question could be raised as to whether the high recurrence rate seen in those patients treated with less than 3,000 rads might be due to a large number of Stage III and IV cases who received low doses because they already had advanced disease when first seen. Such patients would be expected to have a high incidence of reseeding back into treated areas and thus a high recurrence rate. However, the recurrence rates we observed in patients who were initially Stage I and II (Fig. 7) were very similar to the rates in patients with all stages of disease (Fig. 6). A recurrence was approximately twice as likely to take place in a field treated with 2,000–3,000 rads as in one treated with more than 3,000 rads. Recurrence rates reported by other authors who gave doses of 3,000–4,000 rads are 6 per cent,[10] 19 per cent,[5] and 4.4 per cent.[6] Differences in methods of analysis account for some of the variability in the rates reported.

Although the number of cases are small, the data on lymphosarcoma and reticulum cell sarcoma suggest that when these diseases are localized, treatment with radiation therapy may also produce a cure of disease. However, these disorders appear to differ in their behavior from Hodgkin's disease in a number of ways: (1) Fewer cases presented as localized disease; (2) no patient with Stage II disease survived, suggesting that these disorders disseminate much earlier than Hodgkin's disease; and (3) the majority of patients had dissemination as the first sign of reactivation. Only 1 of 5 patients had an extension to an immediately adjacent area. Four patients had extensions to non-adjacent areas. Similar data regarding spread of lymphosarcoma and reticulum cell sarcoma were obtained by Han and Stutzman,[4] Scheer,[15] and Peters.[12] The latter also observed a much greater survival rate in Stage I than in Stage II patients. Prophylactic irradiation was found not to be of benefit by Peters in lymphomas other than Hodgkin's disease, which she felt was due to the propensity for distant spread. In a large series of patients Easson has shown that survival rates in other lymphomas that are localized equal those of localized Hodgkin's disease.[2] These patients were not staged in a detailed fashion, however, and it is possible that most of them represent Stage I disease. He implies that few if any cases of abdominal disease were considered localized. Retroperitoneal lymphomas comprise 5 of our 8 cases of Stage II disease.*

In any event, treatment of Stage I lymphosarcoma and reticulum cell sarcoma with radical radiation therapy seems indicated. How extensive the treatment field should be remains in doubt.

CONCLUSIONS

1. Hodgkin's disease frequently presents as a localized disorder, spreads in a contiguous fashion, and is curable in over 50 per cent of such cases with radical radiation therapy.

2. Other lymphomas may be equally curable when the disease is confined to one anatomic region (Stage I). However, such cases comprise only about 10 per cent of the total. Furthermore, these diseases are more apt to develop widespread dissemination rather than contiguous extension.

3. Extended field therapy involving treatment of clinically uninvolved lymph node areas reduces the incidence of reactivation, although improved survival rates could not be demonstrated in this series.

4. Recurrence rates in treated fields are inversely related to the dose of radiation delivered. True recurrences were not seen

* Because of the extent of the disease, retroperitoneal lymphomas were classified as Stage II.

above 3,000 rads. The over-all recurrence rate was approximately 25 per cent in both Hodgkin's disease and other lymphomas receiving 3,000 rads or more.

SUMMARY

Two hundred and seventy-eight patients with malignant lymphomas seen in the Department of Radiation Therapy at the Yale-New Haven Hospital during the years 1958–1966 were studied. Of 142 patients with Hodgkin's disease, 79 had Stage I or II disease, 54 of whom received radical radiation therapy (tumor doses in excess of 3,000 rads to all known disease with intent to cure). The cumulative survival rate of those radically treated was 82 per cent at 5 years counting all patients and 55 per cent including only those living and free of disease. Stage I and II patients not radically treated had a cumulative survival rate of 35 per cent at 5 years but no survivor was free of disease. Reactivations occurred in 55 per cent of patients with Hodgkin's disease but usually consisted of extensions to immediately adjacent lymph node areas. Sixteen such extensions in 9 patients were successfully treated. Local control of disease was achieved in approximately 75 per cent of fields treated with doses greater than 3,000 rads. Fields receiving 2,000–3,000 rads were controlled only 45 per cent of the time.

Of 136 patients with lymphosarcoma, reticulum cell sarcoma and follicular lymphoma, 36 had Stage I and II disease, 20 of whom received radical radiation therapy. Seven of 12 Stage I patients survived free of disease for periods of 3 to 8 years. No Stage II patient survived. In contrast to Hodgkin's disease, the other lymphomas tend to be more generalized when first seen and usually disseminate rather than spread in a contiguous manner. If confined to one anatomic area, however, they appear to be curable with radical radiation therapy.

Morton M. Kligerman, M.D.
Department of Radiology
Yale University School of Medicine
333 Cedar Avenue
New Haven, Connecticut 06510

REFERENCES

1. BERKSON, J., and GAGE, R. P. Calculation of survival rates for cancer. *Proc. Staff Meet. Mayo Clin.*, 1950, *25*, 270–286.
2. EASSON, E. C. Long-term results of radical radiotherapy in Hodgkin's disease. *Cancer Res.*, 1966, *26*, 1244–1247.
3. FAYOS, J., HENDRIX, R., MACDONALD, V., and LAMPE, I. Hodgkin's disease: review of radiotherapeutic experience. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1965, *93*, 557–567.
4. HAN, T., and STUTZMAN, L. Mode of spread in patients with localized malignant lymphoma. *A.M.A. Arch. Int. Med.*, 1967, *120*, 1–7.
5. JACOBS, M. L., and MARASSO, F. J. Lymphomas: relationship between dosage and recurrences. *Radiology*, 1964, *83*, 106–107.
6. KAPLAN, H. S. Evidence for tumoricidal dose level in radiotherapy of Hodgkin's disease. *Cancer Res.*, 1966, *26*, 1221–1224.
7. KAPLAN, H. S. Long-term results of palliative and radical radiotherapy of Hodgkin's disease. *Cancer Res.*, 1966, *26*, 1250–1253.
8. KAPLAN, H. S. Radical radiotherapy of regionally localized Hodgkin's disease. *Radiology*, 1962, *78*, 553–561.
9. MOLANDER, D. W., and PACK, G. T. Management and survival of 883 patients with malignant lymphoma. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1965, *93*, 154–159.
10. NOETZLI, M., and SHELINE, G. E. Local recurrence in lymph nodes irradiated in Hodgkin's disease. In: Progress In Radiation Therapy. Volume II. Edited by F. Buschke. Grune & Stratton, Inc., New York, 1962, pp. 188–194.
11. PETERS, M. V. Prophylactic treatment of adjacent areas in Hodgkin's disease. *Cancer Res.*, 1966, *26*, 1232–1243.
12. PETERS, M. V. Contribution of radiation therapy in control of early lymphomas. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1963, *90*, 956–667.
13. ROSENBERG, S. A. Report of the Committee on the Staging of Hodgkin's Disease. *Cancer Res.*, 1966, *26*, 1310.
14. ROSENBERG, S. A., and KAPLAN, H. S. Evidence for an orderly progression in spread of Hodgkin's disease. *Cancer Res.*, 1966, *26*, 1225–1231.
15. SCHEER, A. C. Course of Stage I malignant lymphomas following local treatment. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1963, *90*, 939–943.
16. ULTMANN, J. E., CUNNINGHAM, J. K., and GELLHORN, A. Clinical picture of Hodgkin's disease. *Cancer Res.*, 1966, *26*, 1047–1062.

CURATIVE TREATMENT OF HODGKIN'S DISEASE*

By JOHN F. HYNES, M.D.
WILMINGTON, DELAWARE

THIS relatively small series of patients with Hodgkin's disease is presented for several reasons. First, the plan of treatment has varied little over the past 30 years. Second, all the patients have been treated and followed by the author, with consultation as necessary, save for a clinical group to be described. Third, curative treatment was our objective and has been attained in a reasonable proportion of cases. Fourth, kilovoltage irradiation, rather than megavoltage, has been the only modality available to the author. Since the majority of therapeutic radiologists still must depend on kilovoltage therapy, it seems worthwhile to emphasize its usefulness. Recently, Fuller[3] flatly stated that megavoltage therapy is the only proper irradiation for Hodgkin's disease, an opinion not substantiated as yet.

In 1935, dissatisfied with the twin concepts that Hodgkin's disease is inevitably fatal, and that radiation therapy is palliative only, the author attempted to devise a technique of curative irradiation. By great good fortune, the first attempt was successful: the patient has had no recurrence after 33 years. In 1937 Gilbert's report at the 5th International Congress of Radiology,[4] from which we adopted his term of "segmental radiation therapy," encouraged us to continue the technique. A few years later, in 1950, Peters[11] first published the technique of "proximate" radiation therapy, and in 1953, with Dr. R. W. Frelick, I described my technique,[5] which was similar to hers and to Gilbert's.[4] In 1955, I wrote on the "Radiocurability of Malignant Lymphoma"[6] which may have been the first article to claim that this disease can be cured. Easson[1,2] has written provocative articles on the cure of Hodgkin's disease; Kaplan[7,8,9] has also taken up the cudgels for curative treatment.

My approach to the treatment of Hodgkin's disease was based on the knowledge that many, but not all, cases are very radiosensitive, many regress with local or regional treatment but recur elsewhere; most had more widespread disease than could be recognized clinically. A negative chest roentgenogram cannot rule out centrally placed lymph nodes 2–3 cm. in diameter; a negative abdominal examination cannot rule out para-aortic lymph nodes. The diagnostic techniques today are far better than those of 1935, but even with tomograms of the chest and with retroperitoneal lymphadenography, freedom from disease in these areas cannot be proved beyond the 90th percentile of probability. The mesenteric lymph nodes still cannot be demonstrated without laparotomy, and perhaps not even then in the obese patient.

Another fact, in 1935 as today, is that cervical lymphadenopathy, the presenting sign in 75 per cent of Hodgkin's disease patients, has a very different significance if the major cervical lymphadenopathy is supraclavicular in location. I am totally convinced that all Hodgkin's disease presenting in the supraclavicular fossa is secondary to disease below the clavicles: mediastinal, retroperitoneal, or possibly visceral. When Hodgkin's disease (or any other lymphoma) appears in the lower neck and *later* involves the pharynx or tonsil, the latter must be considered a tertiary, not a primary manifestation. Finally, if Hodgkin's disease is found in an axillary or inguinal lymph node only, we have to assume that this is secondary to disease elsewhere, not "primary" or "localized."

Upon the basis of these observations, it seemed logical to treat *all* the major lymph node regions. If, as the evidence seemed to indicate, the patient with cervical Hodgkin's disease already had metastases *to* ad-

* Presented at the Fiftieth Annual Meeting of the American Radium Society, Miami Beach, Florida, April 7–11, 1968.

jacent lymph nodes[11] or *from* distant, as retroperitoneal lymph nodes,[6] why not try to treat the whole disease? All the major lymph nodes? Could the patient tolerate such treatment? Very cautiously, in favorable patients (young, strong, without systemic symptoms), this method of treatment was attempted, and they survived, and some are cured. With more experience it was extended to every possible case—Stage I, II or III—abandoning such segmental therapy only when it was failing to benefit the patient. For example, a patient with Stage IIIB Hodgkin's disease had segmental radiation therapy 11 years ago. Six months after treatment, with systemic symptoms, he required irradiation of the liver and spleen. Six or 7 years later he had a radical neck dissection for recurrent disease. A few months ago recurrent systemic symptoms prompted a restudy and disclosed mediastinal and retroperitoneal lymphadenopathy, which is now being irradiated.

Quite obviously our results, as those of all authors, will depend on the stage of the disease under treatment. Elderly obese patients will not do as well as young lean patients. Those with systemic symptoms do poorly (but see case record above); as others have noted, elderly women do poorly. A brief breakdown of my experience is provided in the tables—not that they are statistically significant in a series of this size: they are inserted to indicate that this is an average, not a selected group. It is highly probable that some of the Stage I cases of 10 or 20 years ago would be reclassified at a higher level with our present diagnostic methods (Tables II and V).

The treatment to be described evolved slowly over several years. Some of the successful cases would now be considered undertreated. At the time, it was a radical approach. In a sense it still is, despite the dosage levels now being recommended.[2,7–10] The difference probably lies in the lesser biologic effect of megavoltage therapy. The authors who advocate dosage levels of 3,000–4,000 rads apparently get little more bone marrow depression than can be attained with much more modest dosages of orthovoltage therapy.

In any event, no patient treated by the technique to be described had irreversible bone marrow depression. As a possible by-product, vertebral or spinal cord involvement by extradural or vertebral tumor in patients who had segmental irradiation has never been encountered, perhaps because the entire spine falls within the treatment fields. There has been, of course, extradural or vertebral tumor with cord compression as a presenting symptom in previously untreated patients.

MATERIAL AND METHODS

In all cases, histologic confirmation of diagnosis was obtained. Three groups of patients are considered:

(1) All patients admitted to the Carpenter Clinic, a tumor clinic in a general hospital, from June, 1935 to June, 1950, except as stated below, are included.

(2) All patients referred to me in private practice from June, 1950 to June, 1966 are included. (Same exceptions.)

(3) All patients treated in the Carpenter Clinic, from 1950 to 1962, are separately considered, since they had, in general, the same sort of treatment previously instituted. These cases are discussed in less detail since their records are less accessible, and are not included in the actuarial survival table; yet their survival is statistically about the same as my personal series, since their treatment was much the same. They are included to show that my personal series since 1950 is not a highly selected one (Tables I and IV).

The exceptions mentioned above are those few patients (9 in all) who had a long history of Hodgkin's disease prior to admission. Some of them had been under treatment elsewhere for many years, and had a 5 to 10 year history of proven Hodgkin's disease before admission. One such patient, with proven Hodgkin's disease for 9 years,

survived a total of 21 years. These patients are not included in the analysis of survivals as their inclusion would have no effect on the statistical results. All previously non-irradiated patients have been included, including one very ill patient who died within 2 weeks of admission. It might be of interest to consider separately the so-called "early cases." Table v tabulates the stage of the patients disease on admission; the series is too small for this to be significant but it indicates that these were not all early cases.

Following biopsy diagnosis and routine studies (blood cell count, chest roentgenography, and, during the past few years, lymphadenography, chest tomography, bone marrow aspiration and liver function tests, some of which were not available in 1935), the treatment plan is set up. The eventual aim is to treat all major lymph node complexes. Initially, the areas of known involvement and the adjacent lymph nodes are treated. After 2 or more months lymph nodes not proven to be involved are given treatment (not "prophylactically," but as having known but minimal disease). Such treatment necessarily involves cervical, axillary, mediastinal, para-aortic, iliac and inguinofemoral lymph nodes (Fig. 1). At first the spleen was included, but it was soon omitted in the absence of splenomegaly, and also omitted are such peripheral lymph nodes as epitrochlear, popliteal, occipital and the like, unless there is palpable disease. Usually the lymph nodes on one side of the diaphragm are

Table I

Sex and Age Distributions: Hodgkin's Disease 1935–1966

A—Personal Series		B—Carpenter Clinic Series	
Sex	Median Age	Sex	
Males 42	37	Males 27	
Females 32	47.5	Females 15	
Total 74	41.5	Total 42	
M/F ratio 4:3		M/F ratio 2:1	

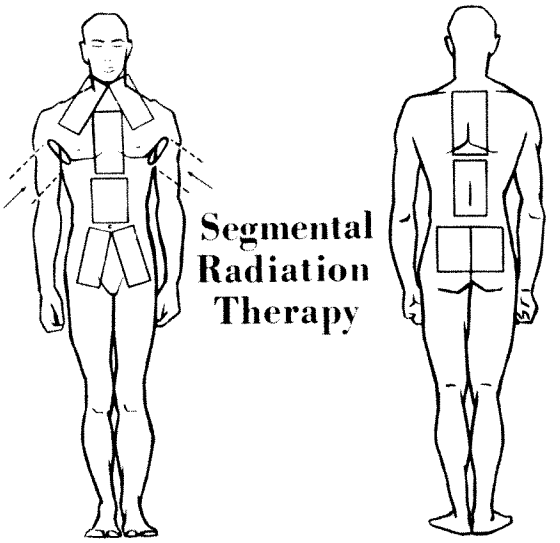


Fig. 1. Fields of treatment used in Hodgkin's disease.

treated in the first series, those on the other side after a rest period. Exceptions are made of course: in the patient with left supraclavicular lymph nodes and a positive lymphadenogram of retroperitoneal lymph nodes, treatment will be started to the abdomen and left neck. Using kilovoltage therapy (200 kv., 280 kv.) patients will tolerate 1,200 r (air) up to 1,800 r (air) through each large (150–200 sq. cm.) field used. In general, the 1,200 r dose is used where no lymph nodes are palpable or visible in the roentgenogram, the higher dose over clinically diseased lymph nodes. For superficial lymph nodes where the air dose is often less than the tissue dose (considering an average of 25 per cent backscatter in large fields) 1 field is employed. For deeper lymph nodes (axillary apical, mediastinal, retroperitoneal), 2 opposing fields, each contributing about 50 per cent of the total tissue dose, are considered necessary.

As previously noted, these dosage factors refer to kilovoltage therapy in the 200 to 280 kv. range, with a half-value layer of 1.0 to 1.3 mm. Cu, not to megavoltage therapy. Following the initial course of treatment, above or below the diaphragm, patients usually show mild leukopenia, with little change in hemoglobin or red blood cells. If

TABLE II

SURVIVAL WITH RESPECT TO AGE (64 CASES PRIOR TO JUNE 1962)

	Male				Female			
	5 Years		10 Years		5 Years		10 Years	
	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent
Under median age	14/19	70	9/17	53	9/11	80	6/14	60
Over median age	8/19	25	3/16		1/15		0/14	
Total	22/38	58	12/33	36	10/26	40	6/28	21

treatment is given at the rate of 200 r (air) through 2 of 6 fields daily to a total of 1,200 r (air) or slightly more in 3 to 4 weeks, radiation sickness is rarely a problem. The second course (to grossly not demonstrable lymph nodes, or to proven lymph nodes in Stage III patients) is more likely to cause leukopenia. This course is interrupted if the white blood cell count drops to 2,000 or below and resumed after a rest period of 2–4 weeks. Moderate anemia may occur after the second series: iron by mouth for a few months is usually adequate treatment. Thrombocytopenia from treatment has been no problem, and no patient treated by this technique has developed irreversible bone marrow damage, although the treatment includes cervical, dorsal and lumbar vertebrae, sternum, central ribs and central pelvis. Occasionally we try to protect the ovaries of young women with a central suprapubic and sacral shield not more than 8 cm. in diameter, if such a shield does not protect the involved iliac chain. Usually they develop amenorrhea from scattered radiation for at least a year. It should be noted that no patient given the full treatment described above, cured or not of his lymph node disease, has yet developed extradural compression of the spinal cord, or vertebral Hodgkin's disease affecting the spinal cord. Should a patient need bone marrow studies after irradiation by this plan, aspiration or trephine biopsy of the lateral ilium is recommended rather than of the irradiated sternum or vertebral spine.

It is difficult to explain why dosage of 1,200 to 1,800 r with kilovoltage x-ray therapy seems to produce about as many long survivors as does much higher dosage with the megavoltage therapy now recommended. Perhaps the higher voltages have less biologic effect; apparently the degree of bone marrow depression is no greater than the patients in this study have had with what seems to be much lower doses than others recommend.[2,7–10] Other evidence of damage, to bones, spinal cord, lungs and kidneys have not been encountered. A few patients, after treatment, had persistent recurring febrile episodes, attributed to residual active Hodgkin's disease, and were given vigorous chemotherapy. Often autopsy showed little or no residual Hodgkin's

TABLE III

SURVIVAL WITH RESPECT TO TYPE OF RADIATION THERAPY 1935–1962

	5 Years	10 Years
Local or regional	3	0
Mild segmental (1,000 r)	2	0
Moderate segmental (1,000–1,800 r)	24	15
Incomplete moderate segmental (½)	4	1

TABLE IV

SURVIVAL OF CARPENTER CLINIC SERIES

	No.	5 Years	10 Years
1950–1957	19	4	4*
1950–1962	30	8†	

* 3 had segmental, 1 had regional therapy.
† 6 had segmental therapy.

disease, but rather renal or pulmonary infections with resistant and/or bizarre organisms presumably encouraged by steroids and chemotherapeutic agents.

RESULTS

The author's personal series of 74 patients consists of all those patients treated from July, 1935 to June, 1950 in the Tumor Clinic of a General Hospital, and of those treated from July, 1950 to June, 1966 in private practice. The stage of disease has been about the same in these 2 groups, and there seems to be no selection. For comparison with the second half of my personal cases, the results of my successors in the same tumor clinic from 1950 to 1962 (as of June, 1967, the end point of my personal series) have been reviewed in less detail. Since the same general plan of therapy was followed by my successors, the results should be, and are, approximately the same. The survival of my cases from 1935 to 1967 is calculated by the life-table actuarial method (without correction for normal mortality by age), with the help of an independent biostatistician.* As noted previously, 9 cases with a long history of treatment elsewhere are excluded. Their inclusion would make little difference in the statistics calculated from apparent onset—many of them were already 5 year survivors. Staging of patients is now routine; some of the early cases had to be staged in retrospect, and in a few instances the data are lacking, which will explain slight discrepancies in the tables.

As may be seen (Table II; Fig. 2) about half of these patients survived 5 years (the median survival in the textbooks is $2\frac{1}{2}$

* Sidney Pell, Ph.D., biostatistician, E. I. du Pont de Nemours Co.

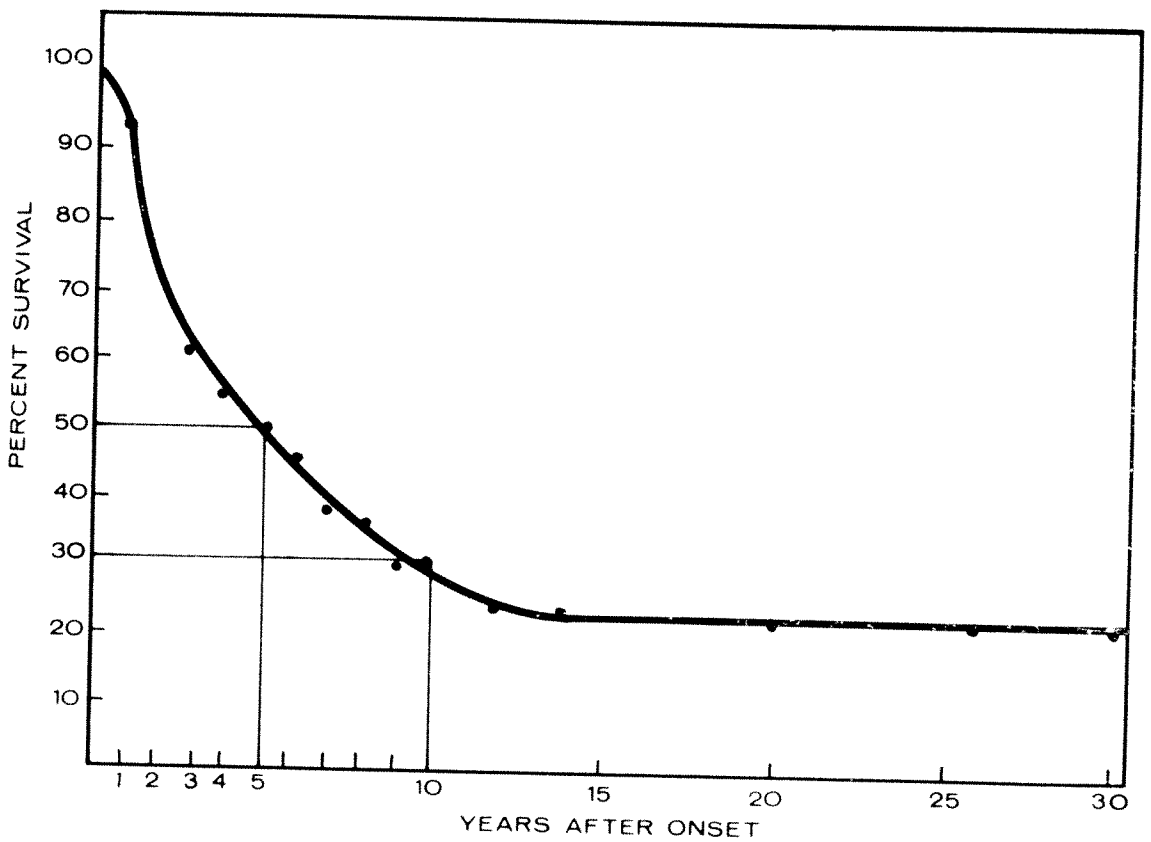


Fig. 2. Hodgkin's disease (1935–1967). Survival from onset; actuarial method.

TABLE V

STAGE OF DISEASE AND SURVIVAL
(62 PERSONAL CASES 1935–1962)

Stage	No.	5 Years	10 Years	15 Years	20 Years
I	6	5	4	4	3
II	19	16	16	4	1
IIIA	12	6	3	1	
IIIB	25	6	2*		

* Alive with disease.

years). A third of the patients survived 10 years—those with no recurrence for 10 years still survive 10 to 30 years. Several patients died from known intercurrent disease during the first 10 years after treatment (miliary tuberculosis, myocardial infarction [2], pyelonephritis with uremia) with no Hodgkin's disease found at autopsy.

In the personal series (74 patients), 42 were males and 32 females, a ratio of 4:3. The Carpenter Clinic from July, 1950 to June, 1966 admitted 27 males and 15 females, approximately a 2:1 ratio. The median age on admission of the personal series was 41.7 years; 37 years for men, 47.5 years for women (Table I). As others report, younger patients have a better prognosis. Of males under the median age, 14 of 19 (70 per cent) survived 5 years and 9 of 19 (53 per cent), 10 years. Of the females under the median age, 80 per cent survived 5 years, only 1 over the median age lived 5 years and none for 10 years (Table II).

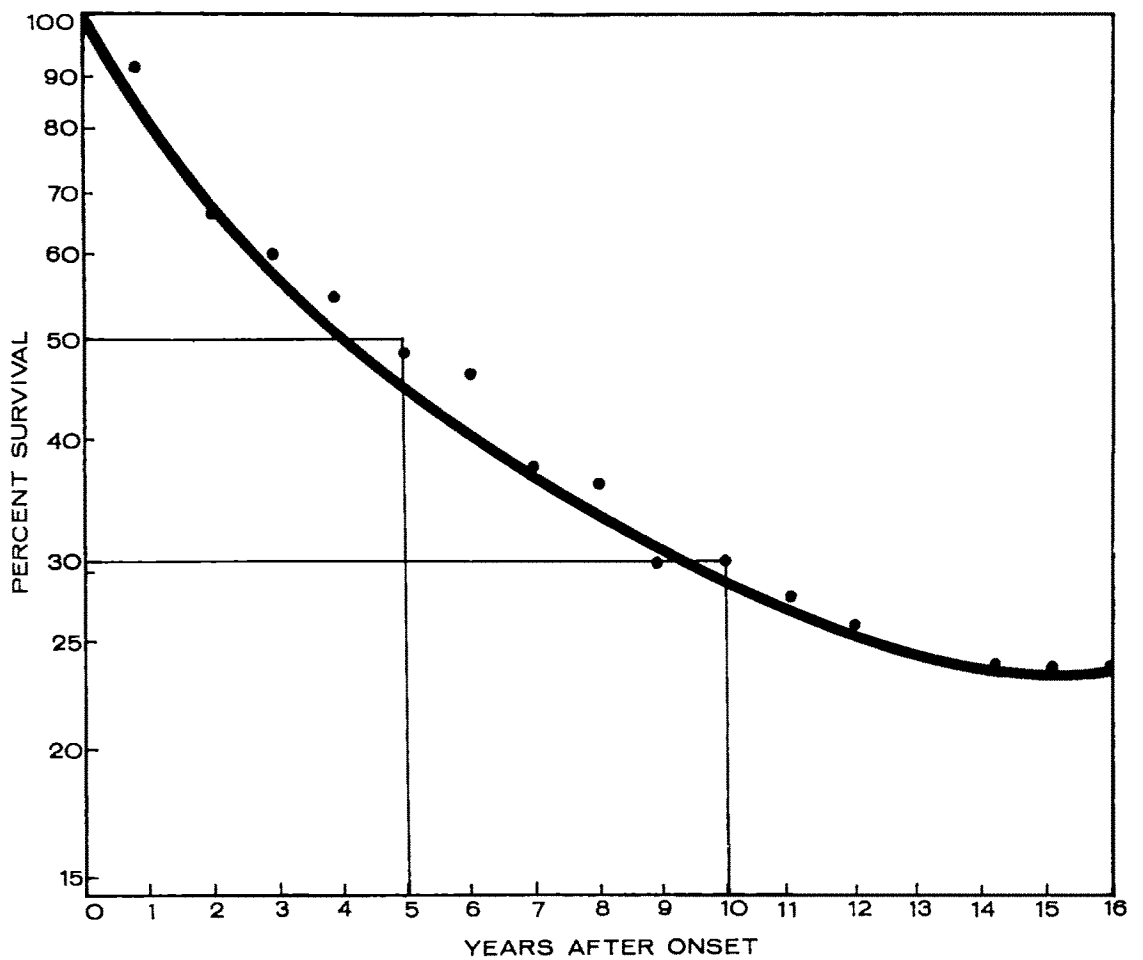


FIG. 3. Hodgkin's disease (1935–1967). Survival from onset; life-table method: semilogarithmic scale.

Of 64 patients treated before June, 1962, 33 lived 5 years (50 per cent), and 16 of 57 admitted prior to June, 1957 were living in July, 1967. Only 2 of these patients have required repeated treatment; the others are all apparently cured. Analysis with respect to the type of therapy used indicates that local or regional treatment yielded 3 survivors for 5 years, none for 10 years. Segmental therapy in dosage under 1,000 r (air) per field yielded 2 survivors for 5 years, none for 10 years. Segmental therapy with moderate dosage of 1,000–1,800 r (air) yielded 24 survivors for 5 years and 15 for 10 years. A few patients had incomplete segmental therapy (one side of the diaphragm only) with 4 survivors for 5 years and 1 for 10 years (Table III).

Among the parallel series from the hospital Tumor Clinic, 4 of 19 patients treated from 1950–1957 have survived 10 years; 1 had regional treatment only, 3 had segmental therapy. Of 30 cases treated from 1950–1962, 8 lived 5 years; 6 of these had segmental irradiation (Table IV).

When we consider the stage of disease and survival, admitting the inaccuracy of the staging methods earlier in this series, we find as expected that patients with limited disease do well. Table V shows that 4 of 6 Stage I cases survived 10 and 15 years; 16 of 19 Stage II cases lived 5 years and 10 have been well 10 years. Most encouraging is that 6 of 12 Stage IIIA cases lived 5 years and 3 are living 10 or more years. Only 6 of 25 Stage IIIB patients lived 5 years and 2 of those are living with disease more than 10 years.

Figures 2 and 3 demonstrate the survival curve of my personal experience from 1935–1966; 74 patients followed 1 year or longer, using the life-table method. Figure 1 depicts diagrammatically the fields used in this technique.

SUMMARY

The technique of segmental therapy used by the author is described.

Hodgkin's disease can be treated successfully by kilovoltage roentgen therapy.

A 5 year survival rate of 50 per cent and a 10 year survival rate of 30 per cent is reported.

No patient in this series subsequently developed spinal cord compression from vertebral or extradural tumor.

No patient free of disease for 10 years has developed recurrence in up to 33 years. All patients have been followed up to July, 1967 or to death.

While it is not the subject of this report, the same technique of therapy yields similar results in the treatment of lymphosarcoma.

1303 Delaware Avenue
Wilmington, Delaware 19806

REFERENCES

1. Easson, E. C., and Russell, M. H. Cure of Hodgkins's disease. *Brit. M. J.*, 1963, *1*, 1704–1707.
2. Easson, E. C. Long term results of radical radiotherapy in Hodgkin's disease. *Cancer Res.*, 1966, *26*, 1244–1247.
3. Fuller, L. M. Discussion: long-term results of radical radiotherapy in Hodgkin's disease. *Cancer Res.*, 1966, *26*, 1248–1249.
4. Gilbert, R. Radiotherapy in Hodgkin's disease: malignant granulomatosis. Am. J. Roentgenol. & Rad. Therapy, 1939, *41*, 198–241.
5. Hynes, J. F., and Frelick, R. W. Roentgen therapy of malignant lymphoma with special reference to segmental radiation therapy. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1953, *70*, 247–257.
6. Hynes, J. F. Radiocurability of malignant lymphoma. *Acta Unio internat. contra cancrum*, 1955, *11*, 514–525.
7. Kaplan, H. S., and Rosenberg, S. A. Treatment of Hodgkin's disease. *M. Clin. North America*, 1966, *50*, 1591–1610.
8. Kaplan, H. S. Radical radiotherapy of regionally localized Hodgkin's disease. *Radiology*, 1962, *78*, 553–561.
9. Kaplan, H. S. Evidence for tumoricidal dose level in radiotherapy of Hodgkin's disease. *Cancer Res.*, 1966, *27*, 1221–1224.
10. Kaplan, H. S. Role of intensive radiotherapy in management of Hodgkin's disease. *Cancer*, 1966, *19*, 356–367.
11. Peters, M. V. Study of survivals in Hodgkin's disease treated radiologically. Am. J. Roentgenol. & Rad. Therapy, 1950, *64*, 299–311.

CUTANEOUS REACTIONS AFTER RADIATION THERAPY*

REPORT OF 7 CASES

By WILLIAM S. MAXFIELD, M.D., *and* WILLIAM P. COLEMAN, M.D.
NEW ORLEANS, LOUISIANA

THE fact that radiation therapy can cause various cutaneous reactions, including erythema multiforme, has been recognized for many years. Holzknecht[11] called attention to this complication of irradiation in 1903. He stated that these eruptions were benign, tending to regress spontaneously. Although radiation dermatitis and associated eczematous dermatitis in the area of treatment at the end of a course of radiation therapy is common, generalized eruptions due to radiation therapy are rare.

Since Schreiner's report in 1924,[19] a number of cases have been recorded.[2,3,8,9,12,13,15–18] In 1952, Davis and Pack[7] collected 32 reported cases of cutaneous reactions after radiation therapy and added 5 of their own. Most reported reactions occurred during orthovoltage therapy, although Davis and Pack reported several cases secondary to 1,000 kv. therapy. The pattern of reactions reported ranged from a mild rash in the area of treatment to fatal purpura[9] and fatal erythema multiforme.[6] Chalmers[6] was able to find only 1 case of cutaneous reaction to radiation therapy in British dermatologic publications.[10] In Burstein's[4] report of 5 cases in 1967, the paucity of recorded cases and lack of information on the subject were underscored.

This report adds 7 cases of cutaneous reaction, including 6 of the erythema multiforme variety and 1 case of severe local reaction, to the 47 previously reported cases (Table 1). Five of the reactions developed after telecobalt 60 therapy; the other 2, one a generalized cutaneous reaction and the other a severe local reaction, occurred during orthovoltage therapy.

REPORT OF CASES

CASE I. A 19 year old white woman was admitted to the Ochsner Clinic on August 4, 1964. A diagnosis of Hodgkin's disease had been made elsewhere by scalene lymph node biopsy. Review of these slides and a roentgenogram of the chest, which showed widening of the mediastinum, confirmed the diagnosis of Hodgkin's disease, Stage 2, involving the cervical lymph nodes and mediastinum. Nitrogen mustard treatment in August, 1964, was followed by moderate shrinkage of the lymph nodes in the neck and mediastinum. Radiation therapy with orthovoltage equipment (280 kv., half-value layer 3.0 mm. Cu) was given to 5 portals in 42 treatments from September 9 to October 20, 1964. She received 3,050 r total tumor dose to the mediastinum and 3,150 r to the left cervical area.

On the 9th day of treatment severe erythema and a macular rash developed in the areas of treatment and persisted for about 47 days (Fig. 1). The patient had no associated symptoms. The hematocrit was 31 per cent and the white blood cell count was 11,200 per ml. When the eruption began, she was taking no medicine. Treatment consisted of topical application of Kenalog ointment 3 times a day. Each time the daily skin dose exceeded 100 r, the rash and erythema would reappear in spite of topical corticosteroid treatment. When last seen on March 25, 1967, the patient was in excellent health with no evidence of Hodgkin's disease.

CASE II. A 54 year old white woman was admitted to the Ochsner Foundation Hospital on February 10, 1966, for breast biopsy. Carcinoma of the breast was diagnosed by needle biopsy. A right radical mastectomy was performed on April 13, 1966, the diagnosis being carcinoma of the breast with metastases to 21 of 23 regional lymph nodes. Orthovoltage therapy (280 kv., 3.0 mm. Cu half-value layer) was given in 17 treatments through 4 separate por-

* Presented at the Fiftieth Annual Meeting of the American Radium Society, Miami Beach, Florida, April 7–11, 1968.
From the Departments of Radiation Therapy and Allergy, Ochsner Clinic and Ochsner Foundation Hospital, New Orleans, Louisiana.

tals, the patient receiving a tumor dose of 3,150 r to the right chest through 2 tangential ports. She also received 2,750 r in 17 treatments to the internal mammary lymph nodes, and 2,750 r to the supraclavicular lymph nodes and the axilla in 17 treatments.

On the 23rd day of treatment, fever, pruritus, erythema, and generalized urticaria developed. Target lesions (Fig. 2), purpura, and eczema were also present. The white blood cell count was 4,250 per ml., and the hematocrit was 39 per cent. In addition, the patient had diffuse erythema on the chest and upper back in the areas of radiation treatment. Before onset of the eruption, she had been taking Tigan. Treatment consisted of topical use of calamine lotion; oral administration of 50 mg. of Benadryl every 4 hours; Alpha-Keri baths daily; topical use of corticosteroid lotion; and 4 mg. of Periactin 4 times daily, by mouth. After 3 days, when the eruption did not adequately subside, she was given corticosteroids parenterally. By the 6th day considerable improvement had occurred with disappearance of the rash by the 9th day. A diagnosis of erythema multiforme due to orthovoltage treatment for malignant disease was made.

The patient died on September 3, 1966, with metastases to the pleural cavity, pericardial sac, liver, and bone.

Case III. A 57 year old white woman was admitted to the Ochsner Foundation Hospital on March 20, 1967. The next day, radical left mastectomy was performed. A diagnosis of carcinoma of the left breast with metastases to 19 of 22 regional lymph nodes had been made. The patient was given telecobalt 60 therapy from April 3, 1967, to May 10, 1967. She received a total of 23 treatments through 2 portals. The skin dose was 4,750 r to the left supraclavicular area and 4,950 r to the internal mammary field on the left for a calculated tumor dose of 4,500 r to each area.

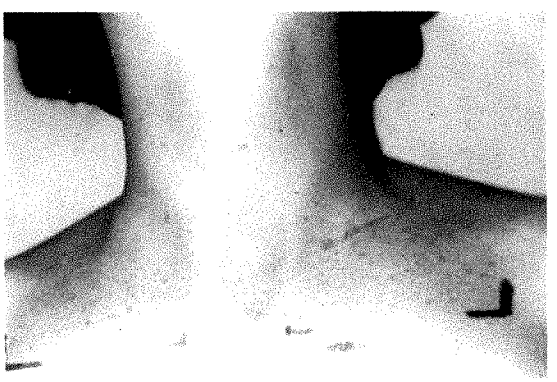


Fig. 1. Case 1. Erythema and urticaria, which developed after the 8th treatment with 280 kv. radiation for Hodgkin's disease.

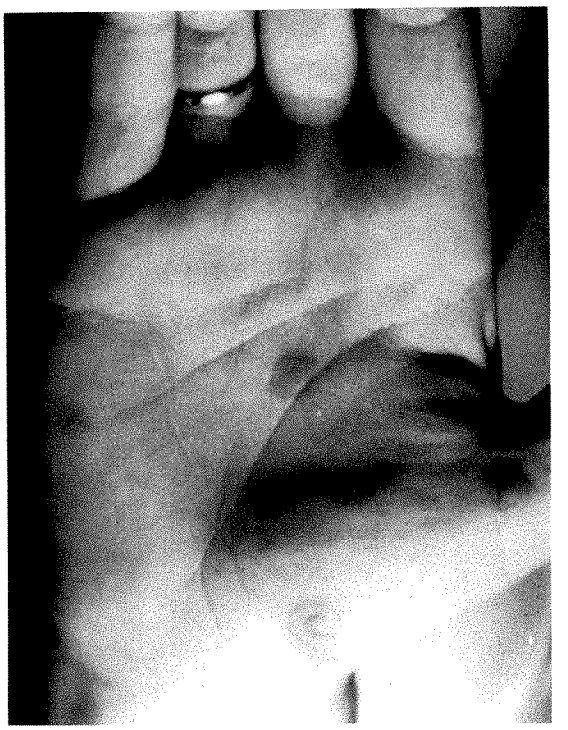


Fig. 2. Case II. Target lesion of erythema multiforme, which developed after the 14th treatment with 280 kv. therapy for carcinoma of the breast.

On the 18th day of treatment, chills, fever, generalized aching, and pruritus developed. Erythema appeared on the neck, chest, and upper part of the back, followed by a generalized morbilliform and urticarial eruption which spared only the face (Fig, 3, *A* and *B*). This lasted about 14 days. The patient was taking Terrastatin. when the eruption began and had had a strontium 85 bone scanning 2 weeks before radiation therapy was started. Her white blood cell count was 10,150 per ml. with 12 per cent eosinophiles, and a hematocrit of 39 per cent.

A diagnosis of erythema multiforme due to telecobalt 60 treatment was made. The rash responded well to treatment consisting of 12 mg. Chlor-Trimeton Repetabs twice daily and application of 0.025 per cent Kenalog lotion, twice daily to the affected areas. The course of radiation therapy was completed without



Fig. 3. Case III. (*A*) Erythema and papules, which developed after the 20th treatment with telecobalt 60 after mastectomy for carcinoma of the breast. Note minimal reaction in supraclavicular and internal mammary areas. (*B*) Note intense reaction in areas of exit of telecobalt 60 portals.

further incident. When last examined on February 20, 1968, the patient was in excellent health with no evidence of malignant disease.

Case IV. A 37 year old white man was admitted to Ochsner Foundation Hospital on September 21, 1967, because of a large mediastinal mass. Left thoracotomy was performed on September 29, 1967. A diagnosis of malignant teratoma, probably arising within the thymus gland, was made. He was treated with telecobalt 60 therapy from October 9, 1967, through November 6, 1967, with anteroposterior and posteroanterior portals, for a total tumor dose of 4,000 r to the left upper pulmonary field and mediastinum, and 3,000 r to the supraclavicular lymph nodes.

On the 20th day of treatment, erythema developed at the site of treatment. Medication at the time the rash developed included a vitamin preparation, Darvon compound, Tigan and Noctec. The only symptom was pruritus. The hematocrit was 40 per cent. The white blood cell count was 7,300 per ml. Six days after completion of the course of radiation therapy, generalized urticaria developed and persisted for about 10 days. Corticosteroids were given orally.

The patient died on January 17, 1968, from widespread metastases involving the liver, spleen, kidneys, bone marrow, and lymph nodes.

Case V. A 39 year old white man was admitted to Ochsner Foundation Hospital on August 23, 1966, for removal of a hydrocele of the left testicle. During hospitalization, enlarged left supraclavicular lymph nodes were detected. A diagnosis of metastatic mucinous adenocarcinoma was made by supraclavicular lymph node biopsy on August 31, 1966. Pancreas scanning indicated that the pancreas was the primary site of malignant disease, and this observation was confirmed at necropsy.

Since the patient was asymptomatic, no treatment was started. In March, 1967, he had

pain in the upper part of the abdomen, and a mass was found in the left supraclavicular fossa. From April 3, 1967, through May 2, 1967, he received 3,650 r total tumor dose to the left supraclavicular fossa, and 4,000 r total tumor dose to the left upper abdomen in 20 treatments, each field being treated each day.

On the 4th day of treatment, generalized urticaria, pruritus and angioneurotic edema developed. The patient was taking Tigan and salicylates when the rash appeared. He also had eaten some strawberries recently, although he had no history of reaction to any food. The hematocrit was 37 per cent, and the white blood cell count was 5,350 per ml. Treatment included subcutaneous administration of aqueous epinephrine; intramuscular injection and oral administration of corticosteroids, Vistaril; and Actifed.

The rash lasted about 6 days. It did not recur when radiation treatment and administration of Tigan were resumed on April 13, 1967. Radiation therapy provided palliation for 4 months but the patient died on October 5, 1967, from metastases to lungs, liver, pleura, and pericardium.

Case VI. A 59 year old white woman was admitted to Ochsner Foundation Hospital on April 13, 1967. She had a left radical mastectomy on April 15, 1967. The diagnosis was infiltrating ductal adenocarcinoma of the breast, 8 of 15 axillary lymph nodes being positive for metastatic carcinoma. Telecobalt 60 treatment was started on April 23, 1967, and completed on May 24, 1967. She received a tumor dose of 4,500 r to the left supraclavicular and internal mammary chains in 23 treatments. On the 10th day of treatment, typical asymptomatic erythema nodosum developed on the legs (Fig. 4).

The hematocrit was 38 per cent; white blood cell count, 5,250 per ml.; sedimentation rate, 51 mm./hr.; and eosinophiles 3 per cent. The patient was taking no medication at the onset of the reaction and had no history of allergic reactions.

The patient was treated with sodium salicylate and Chlor-Trimeton. The rash cleared after 17 days, although radiation therapy was continued.

Case VII. A 63 year old white man was admitted on June 18, 1967, for hematuria. Transurethral biopsy revealed papillary transitional cell carcinoma of the urinary bladder, Grade 2 to 3. Radiation therapy, consisting of 3,000 r to the bladder area in 16 treatments from July 10 to July 31, 1967, with telecobalt 60 therapy through anteroposterior and posteroanterior ports, was completed on July 31, 1967. The patient had had scleroderma since 1960. He had been taking Gantrisin and Tigan.



Fig. 4. Case VI. Erythema nodosum on leg of patient receiving telecobalt 60 after operation for carcinoma of the breast. Reaction developed on 8th day of treatment.

On the 3rd day of treatment, eczematous, erythematous, urticarial and petechial lesions, and angio-edema developed (Fig. 5). The patient also had pruritus. The hematocrit was 38 per cent, and the white blood cell count was 5,150 per ml. A diagnosis of erythema multiforme due to telecobalt 60 therapy was made. Treatment consisted of 8 mg. of Chlor-Trimeton every 8 hours; Vistaril; intramuscular injec-

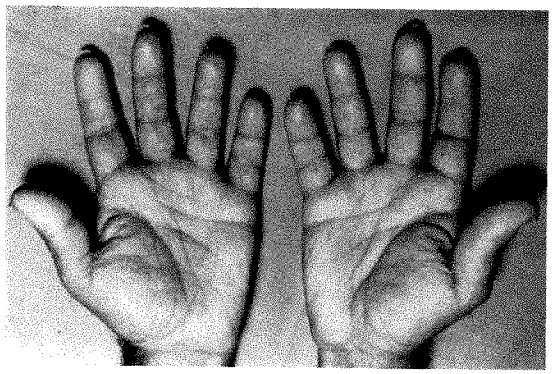


FIG. 5. Case VII. Angio-edema of hand which developed after 16th treatment with telecobalt 60 preoperatively for carcinoma of the bladder.

tion of Kenalog; and Prednisone, orally, for 2 1/2 weeks. Topical soaks were also used. The rash subsided after 16 days.

The patient died October 15, 1967, from infection and gastrointestinal bleeding after cystectomy and ileal loop transplant on September 25, 1967. Neoplastic cells were identified in the cystectomy specimen.

DISCUSSION

The cutaneous reaction to radiation therapy may be a localized or generalized rash, which may appear within 2 days or as long as 42 days after onset of treatment. It usually appears, however, 8 to 21 days after treatment is begun. These reactions to irradiation usually occur in patients being treated for cancer.[7] Fever and constitutional symptoms are common and may require from a few days to a month or more for abatement. The eruption may be erythematous, papular, papulovesicular, lichenoid, bullous, scarlatiniform, purpuric, morbilliform, or exfoliative.[7] As in erythema multiforme due to other causes, the eruption may be accompanied by constitutional symptoms, such as arthralgia, fever, nausea, vomiting, tachycardia, prostration, weakness, pruritus, and radiation sickness. The laboratory data may include evidence of eosinophilia, leukopenia, and mild renal damage.[7]

Although in recent years radiation therapy has been employed mainly for treatment of malignant disease, cancer does not seem to be an essential factor in the development of these rashes. In 1903, Holzknecht[11] reported 5 cases in patients whom he had treated for facial hirsutism, psoriasis, or favus. In 1937, Kautzky[13] described 2 instances in patients treated by radiation for hyperthyroidism and hemolytic jaundice. The fatal case reported by Epstein[9] in 1926 was one of generalized purpura after radiation therapy for cancer of the uterus. The other fatal case, reported by Chalmers[6] in 1959, was in a patient treated for carcinoma of the breast.

Since these reactions resemble drug rashes, and drugs are sometimes used during the course of radiation therapy, many cases may have been overlooked or considered "drug reactions" when they were actually reactions to radiation therapy (Table I). Loewe and Camiel,[15] in 1940, reported cutaneous reactions after radiation therapy in 4 patients who had been receiving barbiturates, but continued use of the barbiturates was associated with involution of the lesions. In 2 patients of Davis and Pack[7] who were given a second course of radiation therapy, the generalized cutaneous eruption recurred. Schreiner[19] and Mac cagno[16] had similar experiences. One of Burstein's patients[4] had recurrence of the cutaneous reaction after diagnostic roentgenography of the cervical spine 8 years after the reaction to radiation therapy. This would seem to be strong evidence in favor of radiation therapy as a cause of the eruption in these cases.

Two of our patients were not taking drugs when the cutaneous reaction occurred. The other patients were taking drugs which could have caused or contributed to the reaction. In Case V, however, the antinauseant was taken again without appearance of a rash. In all of our patients the cutaneous reaction was most severe in the field of treatment or area of exit of the port. This observation, which has also been made by others, would support the position that these reactions are due to radiation, or if not, that the radiation contributed to the reaction. The antinauseant routinely pre-

TABLE I

SUMMARY OF CLINICAL FEATURES IN 7 PATIENTS WITH CUTANEOUS REACTION AFTER RADIATION THERAPY

Case	Sex	Race	Age (yr.)	Treated	Radiation Dose, Area Treated	Eruption		Symptoms	Laboratory Data	Duration (days)	Drugs before Eruption	Treatment
						Onset	Type					
I	F	W	19	Hodgkin's disease	280 kv.-HVL: 3.0 mm. Cu: Skin: 3,150 r Tumor: 3,320 r Supraclavicular Mediastinum	8th treatment September 9, 1964 to October 20, 1964 Rash: September 18, 1964	Severe erythema and urticaria in area of treatment	None	WBC-11,200; Hematocrit 31 per cent	47 continued through course of treatment	HN_2 August 7, 1964	Kenalog ointment
II	F	W	54	Postoperative carcinoma of breast	280 kv.-HVL: 3.0 mm. Cu: Skin: 3,200 r Supraclavicular Internal mammary lymph nodes	14th treatment February 15, 1966 to March 16, 1966 Rash: March 8, 1966	Urticaria; erythema; target lesions; purpura; eczema	Fever, pruritus	WBC-4,250 Hematocrit 39 per cent	9	Tigan	Periactin 4 mg.; Benadryl 50 mg.; Calamine lotion; Kenalog ointment; Corticosteroids
III	F	W	59	Postoperative carcinoma of breast	TCo^{60} Skin: 4,950 r Supraclavicular Internal mammary lymph nodes	20th treatment April 3, 1967 to May 10, 1967 Rash: April 29, 1967	Erythema, morbilliform; urticaria	Chills, fever, general aching, pruritus	WBC-10,150; Hematocrit 39 per cent Eosinophiles 12 per cent	14	Bone scanning 2 weeks before; Terrastatin	Chlor-Trimeton; Kenalog lotion
IV	M	W	37	Malignant teratoma of thymus	TCo^{60} Skin: 3,600 r Tumor: 4,000 r Mediastinum	7 days after treatment completed October 9, 1967 to November 6, 1967 Rash: November 13, 1967	Erythema; general urticaria	Pruritus	WBC-7,300; Hematocrit 40 per cent	10	Darvon compound; Tigan, 250 mg. tid. October 25, 1967	Corticosteroids orally
V	M	W	39	Adenocarcinoma of pancreas, metastatic	TCo^{60} Skin: 3,800 r to 4,000 r Tumor: 4,000 r Pancreas, left Supraclavicular	4th treatment progressive to 7th treatment April 3, 1967 to May 2, 1967 Rash: April 7, 1967	Generalized urticaria; angio-edema	Pruritus	WBC-5,350; Hematocrit 37 per cent	6	Tigan and salicylates	Epinephrine; Corticosteroids intramuscularly and orally
VI	F	W	59	Postoperative carcinoma of breast	TCo^{60} Skin: 5,100 r Supraclavicular and internal mammary lymph nodes	8th treatment April 24, 1967 to May 25, 1967 Rash: May 3, 1967	Erythema nodosum	None	WBC-5,250; Hematocrit 38 per cent Eosinophiles 3 per cent; Sedimentation rate 51 mm./hr.	17	None	None
VII	M	W	63	Preoperative carcinoma of bladder	TCo^{60} Skin: 2,500 r Tumor: 3,000 r Pelvis	16th treatment July 10, 1967 to July 31, 1967 Rash: July 28, 1967	Eczematous erythema; angio-edema petechial urticaria	Pruritus	WBC-5,150 Hematocrit 38 per cent	16	Darvon compound; Tigan 250 mg. tid. July 25, 1967	Vistaril; Kenalog topically Corticosteroids intramuscularly and orally

TCo^{60} = telecobalt 60.
HVL = half-value layer.
WBC = white blood cell count.

scribed was Tigan, which one of us (WSM) has prescribed for 7 years without sequelae. Five of our patients with cutaneous reactions were seen during 1967 (3 within 2 months) whereas only 2 were seen during the previous 3 years. During 1967, of 368 patients treated, 39 required Tigan for nausea. From 1961 to 1964 with use of both orthovoltage and supervoltage equipment by one of us (WSM), only 2 mild eruptions were encountered. We have no explanation for the recent increase in cutaneous reactions. The toxic eruption after irradiation is probably due to rapid destruction of the radiosensitive tumor or a cutaneous reaction from absorption of tissue cellular degeneration products. Another possibility is the production of histamine by the radiation therapy.

As the name implies, erythema multiforme is a polymorphous eruption (macules, papules, vesicles, bullae, erythema, and others) of widely varying size and configuration. It is essentially a vasculitic lesion. Classification of this disorder may include the von Hebra or secondary form. The von Hebra type is characterized by regular, recurrent acute attacks, often in spring and autumn, of a symmetrically distributed, exudative, polymorphous, bright or dark red eruption. Individual lesions may be hemorrhagic, ranging from macules to wheals, and may include papules, vesicles, or bullae. In 6 of our 7 patients the reactions occurred in the spring and fall.

Characteristic target lesions (erythema iris) may occur (Fig. 2). Although the eruption may occur in any place on the skin, and mucous membranes of the eyes, mouth, nose and anogenital areas are often affected, it has a predilection for the hands, feet, face, and distal aspects of the limbs.

Secondary types of erythema multiforme include polymorphous, erythematous, vesicular, and bullous toxic eruptions that develop in association with serum sickness and allergic purpura; systemic or visceral diseases, such as infectious mononucleosis, brucellosis, rheumatic fever, typhoid fever, pneumonia, diphtheria, endocarditis, pericarditis, nephritis, and various viral, mycotic, or protozoan infections; immunizations and foreign proteins; contact dermatitis to poison ivy or other allergens; collagen diseases; internal cancer or lymphoma; use of various drugs including penicillin, sulfonamides, and iodides; and, finally, treatment of internal malignant disease with orthovoltage or megavoltage radiation therapy.[1]

When the mucous membranes are involved and systemic involvement is severe, the term, Stevens-Johnson syndrome, is used. This variant causes constitutional symptoms, which may include pain, fever, headache, malaise, prostration, rapid weak pulse, tachypnea, and arthralgia. Leukocytosis, anemia, thrombocytopenia, albuminuria, and red and white blood cells in the urine may appear. Lesions have been demonstrated in the gastrointestinal tract, the genito-urinary tract, heart, joints, lungs, and central nervous system.[14] The Stevens-Johnson syndrome is fatal in a significant number of cases. Panophthalmitis may accompany this form and cause corneal scarring, synblepharosis, synblepharon, blindness, or minor neurologic changes.[14]

Erythema nodosum is often classified as a type of erythema multiforme, to which it is closely related. Lesions are bilateral, symmetric, nodular, and tender. They occur characteristically on the anterior aspects of the lower portion of the legs (Fig. 4). The nodules range from 1 to 5 cm. in diameter. The skin over the nodules is smooth and shiny, and red to bluish brown. Ulceration and exudation are rare or nonexistent, and the mucosa is not affected. The lesions appear in successive crops, and after a few days or weeks undergo slow involution. Because they resemble contusions, the term, dermatitis contusiformis, may be used as a synonym. Although the nodules usually occur on the shins, they may be found elsewhere on the limbs, and on the buttocks or face. This eruption may accompany sarcoidosis or any of the conditions that may be associated with ery-

thema multiforme. Again, the essential lesion is vasculitis involving the deep dermis and subcutaneous tissues.

Treatment of erythema multiforme should include discontinuance of radiation treatment, at least temporarily, administration of antihistamines, topical use of corticosteroids, and, if symptoms are severe, systemic administration of corticosteroids.

Four of our 7 patients died within a few months from advanced disease or complications of further treatment. Therefore, from our experience, cutaneous reaction to radiation therapy is an indication of a poor prognosis. Davis and Pack, however, thought that cutaneous reaction to radiation therapy indicated a favorable prognosis.

SUMMARY

Erythema multiforme as a reaction to irradiation is a distinct clinical entity. We have been able to find reports of 47 previous cases and have added 7 cases of cutaneous reactions after radiation therapy. Two developed after orthovoltage and 5 after telecobalt 60 therapy.

Treatment should include temporary cessation of irradiation, use of topical medications, administration of antihistamines, and systemic administration of corticosteroids if the eruption and systemic symptoms are severe enough to warrant this form of treatment.

William S. Maxfield, M.D.
Radiation Therapy Department
Ochsner Clinic
1514 Jefferson Highway
New Orleans, Louisiana 70121

REFERENCES

1. ANDREWS, G. C., and DOMONKOS, A. N. Diseases of the Skin. Fifth edition. W. B. Saunders Company, Philadelphia, 1963.
2. ARNOLD, H. L., JR. Erythema multiforme following high voltage roentgen therapy: review of literature and report of three cases. *Arch. Dermat. & Syph.*, 1949, *60*, 143–149.
3. BRAY, S. Skin eruption caused by x-ray therapy on endocrine glands. *Brit. J. Radiol.*, 1939, *12*, 312–315.
4. BURSTEIN, H. J. Toxic cutaneous reactions after deep x-ray therapy. *Cutis*, 1967, *3*, 835–840.
5. CASTIGLIANO, S. G. Dermatoses associated with roentgen therapy. AM. J. ROENTGENOL. & RAD. THERAPY, 1941, *46*, 518–531.
6. CHALMERS, D. Fatal case of erythema multiforme following deep x-ray therapy. *Brit. J. Dermat.*, 1959, *71*, 256–260.
7. DAVIS, J., and PACK, G. T. Erythema multiforme following deep x-ray therapy. *A.M.A. Arch. Dermat. & Syph.*, 1952, *66*, 41–48.
8. DEDICK, A. P., JR., and WHELAN, V. M. Generalized skin reaction following deep x-ray therapy. *Radiology*, 1959, *72*, 751–753.
9. EPSTEIN, P. Severe general vascular injuries simulating Werlhof's disease, following intensive local roentgen ray treatment. *Strahlentherapie*, 1926, *21*, 416–418.
10. GOLDSMITH, W. N., and HELLIER, F. F. Recent Advances in Dermatology. Second edition. J. & A. Churchill, Ltd., London, 1954.
11. HOLZKNECHT, G. Fieberhafte Allgemeinerkrankung mit Exanthem bei Röntgendermatitis. *Arch. Dermat. u. Syph.*, 1903, *66*, 71–73.
12. HOPKINS, H. H. Acute disseminated lupus erythematosus; precipitation by roentgen rays and cure with sulfanilamide. *Arch. Dermat. & Syph.*, 1941, *43*, 833–835.
13. KAUTZKY, A. Zur Frage der atypischen Hautreaktionen nach Röntgenbestrahlung. *Strahlentherapie*, 1937, *60*, 439–443.
14. LEWIS, G. N., and WHEELER, C. E., JR. Practical Dermatology. Third edition. W. B. Saunders Company, Philadelphia, 1967, pp. 151–160.
15. LOEWE, L., and CAMIEL, M. R. Exanthem complicating neoplastic disease: its identical occurrence in four cases of carcinoma. AM. J. ROENTGENOL. & RAD. THERAPY, 1940, *43*, 587–596.
16. MACCAGNO, A. Esantema pemfigoide in un linfogranuloma maligno sottoposto a trattamento roentgen-terapico. *Minerva med.*, 1941, *32*, 101–104.
17. MOORE, V. M. Quoted by G. W. Bray. Recent Advances in Allergy. Second edition. P. Blakiston & Son, Philadelphia, 1934, p. 429.
18. PARDO-CASTELLO, V. Allergic cutaneous eruptions after high voltage roentgen therapy. *Arch. Dermat. & Syph.*, 1936, *33*, 886.
19. SCHREINER, K. Rezidivierendes Röntgenexanthem. *Strahlentherapie*, 1924, *16*, 389–393.

DYSTROPHIC EPIDERMOLYSIS BULLOSA*

TOLERANCE OF THE BED AND RESPONSE OF MULTIFOCAL SQUAMOUS CELL CARCINOMAS TO IONIZING RADIATION: REPORT OF A CASE

By ROBERT W. EDLAND, M.D.
MADISON, WISCONSIN

CONGENITAL or hereditary vesiculobullous disorders of the skin are unusual diseases, and reports concerning their association with skin cancer are rare.[3,4,6] Reports in the literature of the effects of ionizing radiation upon the background stroma and neoplasms arising in this stroma cannot be located with reference to the specific entity epidermolysis bullosa. Recently we treated a patient with recessive dystrophic epidermolysis bullosa and recurrent multifocal squamous cell carcinomas of the forearm. Because of the rarity of this disorder and because of several instructive features of this case, we have decided to add it to the literature.

REPORT OF A CASE

At the time of radiotherapeutic consultation, the patient was a 26 year old Caucasian female with a history of epidermolysis bullosa present since birth. Her younger sister also was afflicted with the disease but to a less severe degree. Three brothers and an older sister were not affected. It is of interest that the patient's mother and father were first cousins, although, except for a history of vitiligo in the maternal grandmother, there is no other history of skin disorders in the family's background for at least 4 generations. The family was originally of Germanic origin. There was nothing to suggest porphyria in the family history, and an examination of the patient's urine for breakdown products was negative.

The gestational history was normal and the patient weighed about 10 pounds at parturition. At birth vesicles were noted on the skin and in the oral cavity. The patient had rather marked early feeding difficulties and multiple food allergies. At the age of 6 years, pustules developed and she was placed on large doses of vitamin A topically and orally. During the early years the disease was felt to be of the simplex type since there were short periods when the patient was relatively free of bullae. Catamenia was normal with menarche at age 13. By this time multiple associated skin problems were developing (milia, seborrhea of the face). She began losing her fingernails and toenails and the hair became sparse, thin and brittle. She was noted to have a narrow palate, widened epicanthal folds and intraoral bullae. Her hands developed a claw-like appearance due to the formation of interdigital cicatricial webs secondary to scarring. The skin developed an atrophic papyraceous texture and bullae were noted, especially over pressure points and bone prominences. In 1955 at the age of 14, she was started on systemic steroid therapy. At age 16, she underwent the first of 6 surgical procedures designed to free-up cicatricial bands which had developed in the interdigital webs of her fingers and toes.[1] Poor oral hygiene with marked gum retraction and dental retardation was noted at that time. An autograft and a homograft from a sister were utilized for reconstruction.

In 1963 at the age of 21, the patient developed an ulcer over the medial aspect of the left ankle and a biopsy from this area, which was slow to heal, revealed papillary hyperkeratosis. A biopsy performed 3 months later revealed Grade I squamous cell carcinoma. A few months later a low grade squamous cell carcinoma was biopsied from the dorsum of the right foot. These were removed chemosurgically by Dr. Frederick Mohs, utilizing the zinc chloride fixation technique which he pioneered,[5] and have not recurred. In 1966 at the age of 24, the patient developed 2 ulcerated lesions on the lateral aspect of the right forearm. Biopsy revealed Grade II squamous cell carcinoma, and these were again removed chemosurgically. In April of 1968, the patient noted the development of several recurrent ulcerating lesions in the previously treated bed, and, in addition, a mass appeared in the right epitrochlear region (Fig. 1).

The patient was hospitalized for the tenth

* From the Department of Radiology (Division of Radiotherapy), University of Wisconsin Medical School, Madison, Wisconsin.
Supported by Grant No. CA 06295 from the National Institutes of Health.

time at University Hospitals for evaluation and treatment. At that time she was noted to be a pale, chronically ill appearing female with marked deformities of the hands and feet. The hands were carried in a flexed position and the fingers and toes were now permanently fused in a tight cicatricial mass (Fig. 2). Multiple sores were noted in the mouth and the tongue could not be protruded. Speech and eating, however, seemed relatively unimpaired. There was no complaint of dysphagia or odynophagia. No specific ocular lesions were noted. Mentation appeared normal for a female of this age and there was no evidence of retardation or premature senility. The integument was thin, xerodermatic and atrophic and scars were noted over most of her body (Fig. 3). Areas of confluent pustule formation were also noted. A 1×2 cm. mass was palpable in the right medial epitrochlear region and a similar-sized mass was palpated in the right axilla at the lateral border of the pectoralis major.

A biopsy of the epitrochlear mass was performed which revealed squamous cell carcinoma Grade II, and the patient was referred to the Radiotherapy Center for consultation. Although nothing was actually known about the tolerance of the background stroma and the response of neoplasm arising in such a tumor bed, a trial of radiation therapy was elected since the alternative proposal by the surgeons was amputation. Despite the deformity, the patient could grasp a pencil with a special assist device and write quite legibly and indeed was a part-time student at the University of Wisconsin. Since the chances of developing skin carcinomas elsewhere in her integument were high, and because of the epitrochlear and



Fig. 1. Appearance of the right forearm prior to radiation therapy. Note the 4 cm. raised annular lesion. There were numerous satellite tumors as well.



Fig. 2. A composite photograph showing (left) th appearance of the feet in 1963 and (right) in 196 Note the progressive weblike contractural d formities with resorption of the toes.

axillary lymph node metastases, the prognos was quite grave and the preservation of he limbs for as long as possible appeared desirabl

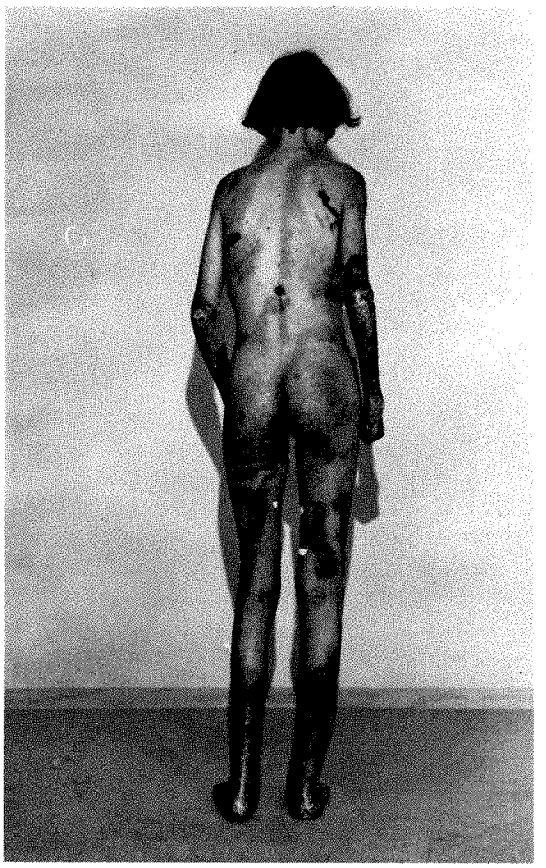


Fig. 3. Full torso view of the patient. Note th marked scarring and areas of fresh vesicule an pustule formations.



FIG. 4. Appearance of the right forearm 6 weeks after completion of the radiation therapy course. Diffuse moist epitheliolysis persists but there is no clinical evidence of residual tumor.

Therefore, despite our lack of information concerning the tolerance of the background stroma, we elected to irradiate the right axilla with a direct, 20 degree oblique cobalt 60 portal at a source-skin distance of 95 cm. (half-value layer 12 mm. Pb). Over a period of 24 days, 5,400 r/air was delivered (18 fractions of 300 r) through a 7×12 cm. portal. The tumor dose at 4 cm. was calculated at 4,600 rads. The weeping, crusting neoplastic lesions of the right forearm superimposed on a thin, atrophic bed were irradiated through a single portal measuring 8×30 cm. This portal, of necessity, extended well above the elbow and included the epitrochlear region. A target-skin distance of 70 cm. was utilized with a half-value layer of 1.5 mm. Cu (250 kvp., 0.5 mm. Cu added filtration). An exposure of 3,220 r/air was administered in 14 fractions over 20 days which resulted in a tumor dose of 4,300 rads at 1 cm. depth.

This technique resulted in a moist desquamation with apparent gross tumor ablation, but the healing or reparative phase was considerably delayed and prolonged. Six weeks after the completion of radiation therapy the reaction was still moist and confluent, and a deeper flexion contracture had developed at the elbow (Fig. 4). Four months after completion of therapy the axillary lymph node was barely palpable, but the forearm reaction was still exudative despite extensive local measures, and a recurrent (persistent) annular lesion was now visible in the previously treated field (Fig. 5). A chest roentgenogram at this time is negative and despite the grave prognosis for survival in the face of axillary metastasis, surgical removal of the right arm is contemplated.

DISCUSSION

Since the basic underlying disorder in dystrophic epidermolysis bullosa appears to be related at least in part to congenital absence or abnormal development of elastic tissue with frequent and easy separation of the epidermal layer from the corium, any physical or traumatic agent applied to this abnormal surface might be expected to enhance these pathologic changes. Also, in the chronic state, the thin atrophic integument might be expected to react with a poor reparative tolerance to ionizing radiation. Indeed the tolerance of the skin and subcutaneous tissues in this rare disorder appears to present a significant therapeutic problem, at least in our very limited experience. It would appear that reduced doses of ionizing radiation must be employed with increased over-all fractionation if reasonable healing without necrosis and preservation of a "functional part" are to be expected, not unlike the theoretical treatment schemas developed in the past for the treatment of Kaposi's sarcoma.[2]

Unfortunately, however, there is no reason to suspect that skin cancers developing in this "tumor bed" have an enhanced radiosensitivity, thereby allowing for "cure" or "ablation" of the malignancy with a lowered tissue dose which might not



FIG. 5. Appearance of the right forearm 3 months later. The moist reaction has not healed despite treatment with several local drying agents. Note the recurrent (persistent) annular lesion which has reappeared.

produce such marked and irreversible changes in the background supporting stroma. The underlying vasculo-connective stroma thus limits the amount of ionizing radiation which can be safely delivered as well as the rate of delivery, and this is the therapeutic "horns of the dilemma." The normal Strandqvist recovery or tolerance curves cannot be applied to the underlying stroma in this disorder.

It is, therefore, our conclusion that neoplasms arising in the background stroma of epidermolysis bullosa should be treated surgically, since the abnormally low tolerance of the tumor bed will not allow delivery of cancerocidal doses of radiation without exorbitant morbidity.

CONCLUSIONS AND SUMMARY

A case report of a patient with multifocal squamous cell carcinomas of the skin developing in the background stroma of dystrophic epidermolysis bullosa is presented together with the results of radiation therapy upon these tumors and the abnormal "tumor bed."

The enhanced damage to the abnormal integument, which has a significantly decreased tolerance to the effects of ionizing radiation, results in a mandatory reduction in time-dose-volume relationships which would appear to render permanent tumor control unlikely in this entity.

Department of Radiology
University of Wisconsin Medical Center
1300 University Avenue
Madison, Wisconsin 53706

REFERENCES

1. Becker, M. H., and Swinyard, C. A. Epidermolysis bullosa dystrophica in children: radiologic manifestations. *Radiology*, 1968, *90*, 124–128.
2. Cohen, L. Dose, time and volume parameters in irradiation therapy of Kaposi's sarcoma. *Brit. J. Radiol.*, 1962, *35*, 485–488.
3. Halpern, L. K. Development of squamous cell epithelioma in epidermolysis bullosa: report of case. *Arch. Dermat. & Syph.*, 1947, *56*, 517–522.
4. Klauner, E. Zungenkrebs als Folgezustand bei einem Fall von Epidermolysis Bullosa (dystrophische Form). *Arch. Dermat. u. Syph.*, 1913, *1*, 71–78.
5. Mohs, F. Chemosurgery in Cancer, Gangrene and Infections. Charles C Thomas, Publisher, Springfield, Ill., 1956.
6. Rasponi, L. Il cancro sull' epidermolisi bullosa distrofica. *Arch. ital. dermat. sif.*, 1950, *23*, 19–37.

A LIGHT ANALOG SYSTEM FOR RADIOTHERAPY PLANNING*

By GERALD S. FREEDMAN, B.M.E., M.D.,† *and* PAUL N. GOODWIN, PH.D.
NEW YORK, NEW YORK

RADIOTHERAPY planning, despite its great importance in the over-all management of malignant disease, is often compromised because of the lack of personnel available for planning and because of the large amount of time often required for more complicated plans. The widely used method of tracing isodose curves and determining their resultant composite is tedious, time consuming and discourages the evaluation of multiple solutions. Moreover, increasing demands on radiotherapy departments as well as the greater need to document treatment planning has often resulted in simplification of treatment alternatives. What is needed is a more efficient planning method to maximize the use of available personnel and optimize planning alternatives. Several methods have been put forth in the past as solutions to this problem; they range from oversimplified, inaccurate or impractical analog methods[3,4,8,9,12] to extremely complex digital computer programs.[11] While computer solutions are elegant, potentially fast and very accurate they are also costly and often not available to smaller hospitals and practices. The proposed method is a light analog of the present isodose curve system. With this method simple, equally-weighted fields including wedged fields and multiple fields can be rapidly evaluated by visual inspection. The system will permit the planner to rapidly evaluate multiple alternatives and produce a final photographic record of acceptable accuracy. Furthermore, more complicated fields including unevenly weighted multiple fields, partial rotation and complete rotation can also be solved with the aid of a proposed light analog unit.

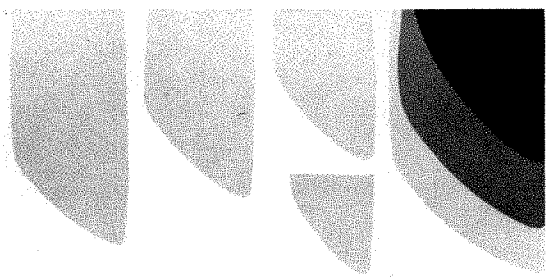


FIG. 1. Using a conventional isodose curve as a guide, a uniform flash isodensity film was cut into sectors as shown on the left. These were then superimposed forming a transparency of isodose curves with film density measurements proportional to the original isodose values.

METHODS AND PROCEDURES

From the conventional isodose curves, isodose transparencies are constructed in a manner similar to that described by Unger.[13] These constitute a light analog of the original isodose curves, as is shown in Figure 1. Before describing their use a short account of their construction follows:

Using Kodak flash isodensity transparencies which can be obtained at specified densities,[7] the shape of conventional isodose curves is cut out and assembled so that the transparent isodose curves vary proportionally to the conventional isodose curves. Or, in other words, the film density as measured by a densitometer is proportional to the isodose values on the conventional isodose curve.

For each port size a transparent analog isodose curve is constructed in this way, giving a family of curves similar to the family of isodose curves. For manual planning by visual inspection at least two isodose curves for each port size must be

* Presented at the Fiftieth Annual Meeting of the American Radium Society, Miami Beach, Florida, April 7–11, 1968.
From the Department of Radiology, the Columbia-Presbyterian Medical Center, New York, New York.
† Present Address: Yale University School of Medicine, New Haven, Connecticut.

made. From each of the originals two or more copies can then be made. Duplicating the originals without contrast distortion requires great skill and care.[6] Once a family of isodose transparencies is obtained, they are then used in the following ways.

TWO FIELDS WEIGHTED 1:1

Figure 2 demonstrates two opposing coplanar fields intentionally displaced to better illustrate the method. Their overlap results in areas of grayness so that regions receiving similar doses of radiation will have similar film densities and appear as areas of equal grayness. Planning is performed on a horizontal viewbox with the appropriate ports superimposed on a cross-section of the patient drawn on transparent acetate. The resulting treatment field, which is easily appreciated by visual inspection, can be varied by changing the angle of interaction of the ports and by selecting the proper port size.

The optimum field configuration is created to match the tumor volume and treatment objectives. When this is achieved another clear sheet of acetate is then placed on top and areas of uniform grayness are enclosed with a wax pencil, thus creating the resultant isodose curves. A permanent record can then be easily obtained using a Polaroid camera with a standard close-up lens. This can then be included on the patient's chart and treatment folder. An example is shown in Figure 3 of a wedge treatment to the head.



Fig. 2. Isodose transparencies made for a 6 mev. linear accelerator with a 5 cm. field are shown as two opposing coplanar fields. They are intentionally displaced to illustrate how the overlapped areas of similar dose have similar film densities.

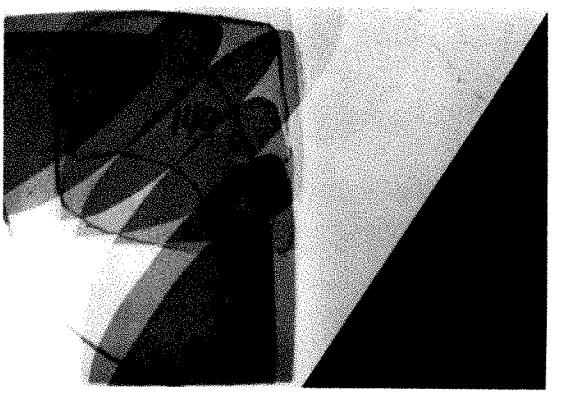


Fig. 3. A Polaroid record of a cobalt 60 wedged field treatment to the frontal portion of the head is shown. The 140 isodose line was drawn on a superimposed transparency and the composite photographed on a viewbox.

While the field shape is determined by inspection, the dose within an isodensity contour is determined by adding the interacting isodose densities. For example, in Figure 3, the 140 isodose resultant curve contains areas of uniform grayness formed by the combination of densities associated with the 80+60, 70+70, and 60+80 isodose lines. Using these same methods solutions to equally weighted fields containing more than two beams can easily be solved. This method will satisfy the needs of most radiotherapy planning problems.

Less common planning solutions which require unequally weighted fields such as 2:1 or 3:1 or even 1.6:1 times the dose from one port compared to the other can be solved with a special planning unit designed for this purpose shown in Figure 8. Furthermore, this unit permits solutions to problems of rotation and partial rotation, or any combination of the above described field interactions. The unit, which produces a photographic permanent record, can also be used for the previously discussed 1:1 fields, thus substituting for a Polaroid

record. In short, the unit can be used for all solutions!

AN EXPLANATION OF THE PHOTOGRAPHIC LIGHT ANALOG

For solutions more complicated than the simple 1:1 fields previously described, it was necessary to develop a system flexible enough to handle all the described possible field interactions. The proposed light isodensity planning unit substitutes film for what the planner has been doing by visual inspection. Until now a transparency has been used in which the analog to maximum radiation had the maximum density. If we were to use this as a negative, interposing it between a light source and a sheet of unexposed film, we would create a conventional exposure. The exposure created is of varying grayness from which one can determine patient dosage. Using the original isodensity transparency and conventional film a reverse image would be created. A single exposure would create a step-wise gray scale with the 100 per cent isodose area now the lowest density and the lowest isodose curve the highest density. This is graphically shown in Figure 4, left side. If such an exposure was made for 1 second and called 100 rads and then another exposure was made for 1 second for another 100 rads, it would obviously be the same as if we had made a single exposure for 2 seconds. The resulting images on the film would have comparable gray areas.

Some consideration should also be given to the type of film used for these exposures. Both the negative forming film as described above or copy film which will reproduce the original density distribution rather than a negative can be used. Figure 4, left and right side, illustrates the advantages and disadvantages of each of these films. It is important to note that when using the transparency which is darkest at 100 per cent (with declining density for lower isodose curves), the summation process produces some ambiguity because the maximum dose area will always result in some intermediate gray value. This is true whether we use copy film or negative film (Fig. 4, left side). However, if we reverse our original transparency, that is, make the 100 per cent isodose level that area of lowest density (greatest light transmission), we gain a distinct advantage. With this method the maximum summed radiation values will be shown as either the darkest or the lightest areas on the superimposed fields, depending on whether we chose copy film or negative film (Fig. 4, right side). The elimination of this ambiguity improves the system and justifies changing our original convention when used in this manner. These isodose transparencies will now be most transparent (lowest density) for areas representing the highest radiation

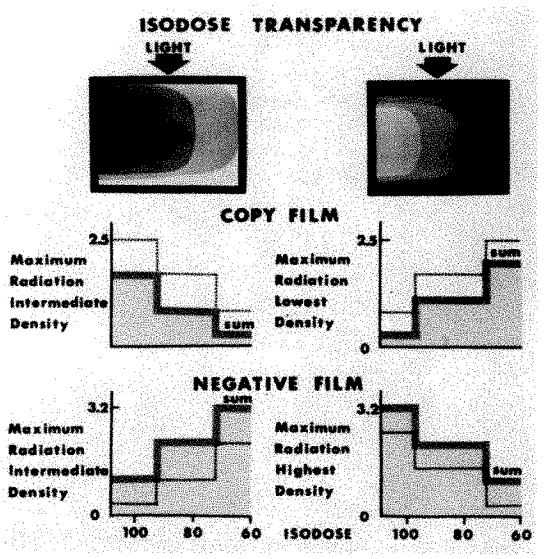


FIG. 4. (*Left*) Using an isodose transparency in which the maximum density represents the entry dose, exposures were made on copy film and negative films as shown by the dotted lines. A second exposure permits more light to strike the copy film thereby decreasing the density at each step and increasing the density on the negative film. In both cases the maximum radiation produces an intermediate density. (*Right*) Using a reverse isodose transparency in which the minimum density represents the entry dose, a single exposure on copy film is shown by the dotted line, a double exposure further lightens (*i.e.*, decreases the density) so that the maximum radiation is represented as the lowest density on the film. On the negative film the maximum density produced by multiple exposures has the highest density.

value rather than the lowest value. An example of the reverse isodose transparency is shown in Figure 5.

An example of a case treated with wedge fields is shown in Figure 6. If we made the first exposure 1 second and then turned the axis of our original transparency 90° for another 1 second exposure, we now would have created crossed wedge fields. Note, however, that only the portion of the exposure which crossed is a double exposure. This double exposed area can be simulated by a 2 second exposure on another part of the same film. This exposure then acts as our calibrated light analog. The grayness in the double exposed area can be converted to rads because it is related to the calibrated analog. This is true because the calibrating curve has been

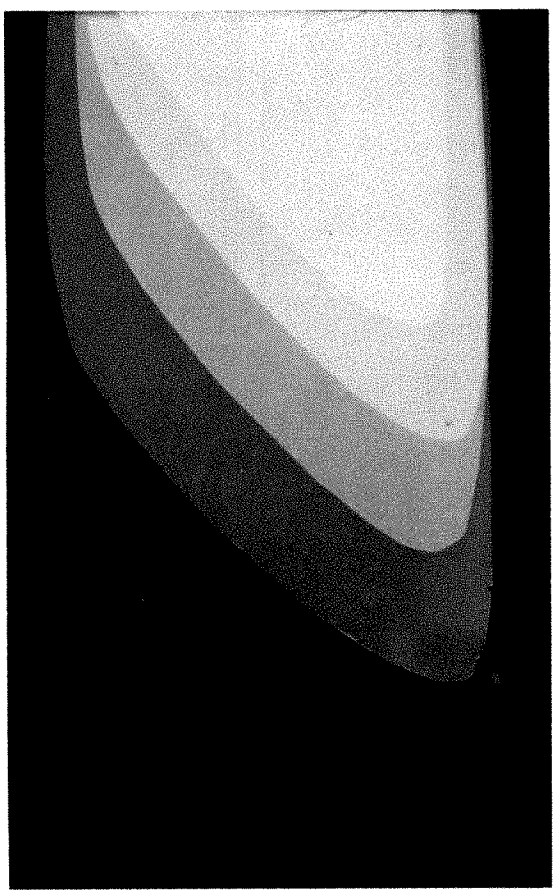


Fig. 5. An example of the reverse isodose transparency for a cobalt 60 wedge is illustrated.

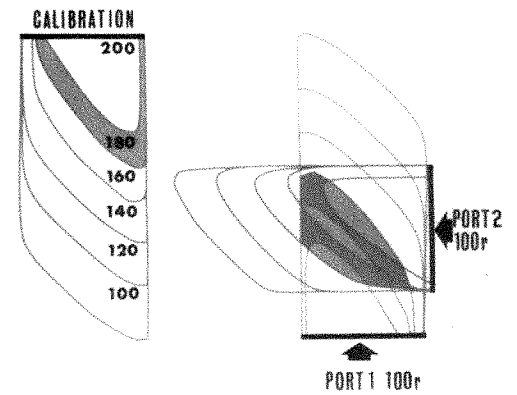


Fig. 6. In the region common to port 1 and 2 the density can be converted to radiation dosage from the calibration curve. If a 1 second exposure represents 100 r, then the 90 per cent isodensity area on the 2 second calibration exposure represents 180 rads. Where the 90 per cent isodensity lines from port 1 and port 2 cross, a grayness is produced equivalent to the 180 rads grayness of the calibration curve.

exposed for a duration equal to the sum of the crossed fields. On Figure 6 it can be noted that when the 90 per cent density (representing 90 rads) of the first field is superimposed on the 90 per cent density (90 rads) of the second field, it will produce a density exactly equal to the 90 per cent density (180 rads) on the calibration field. This fundamental unifying concept in which the planned fields and the calibration curve are exposed on a single piece of film is the key to the light analog system. Using this principle any number of fields static or rotating can be interacted and the density-dose relationship of the final film can be determined independent of all variables (*i.e.*, development time, temperature and solutions, film fogging, etc.) to that film. Since film exposure time is made proportional to patient dosage, a density-dose graph similar to the H&D film response curve can be made. An example of negative film is shown in Figure 7.

A DESCRIPTION OF THE LIGHT ANALOG UNIT

The unit shown in Figure 8 was devised (U.S. patent pending) to permit the solu-

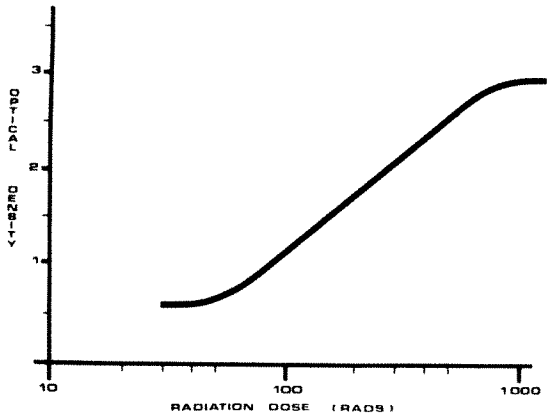


FIG. 7. A modification of the H&D curve shows density as a function of exposure time in which exposure time is calibrated in rads.

tion to all the previously discussed planning alternatives. It has two basic areas: (1) an exposed area on which a rotating platform is connected by a slave arm to an area which is enclosed and light-tight and which contains a similar rotating platform geared to rotate at the same rate. An unexposed film can be introduced into the enclosed area with a special cassette and is free to rotate on the enclosed platform (not shown). Directly above this is an opaque divider which separates the unexposed film from a light source. On this divider between the light and the unexposed film the selected isodose curve can be placed. Exposures of the isodose curve can be made on the unexposed film by timing the light above the divider. The enclosed and the exposed rotating platform are connected by a slave arm. This arm is free to move only in one direction, and when it moves it moves the isodose transparency along the radii of both platforms. When the patient contour is placed on the exposed rotating platform and the slave arm is positioned in contact with the periphery of this contour, the isodose curve in the enclosed housing is positioned over the unexposed film in a similar manner. An

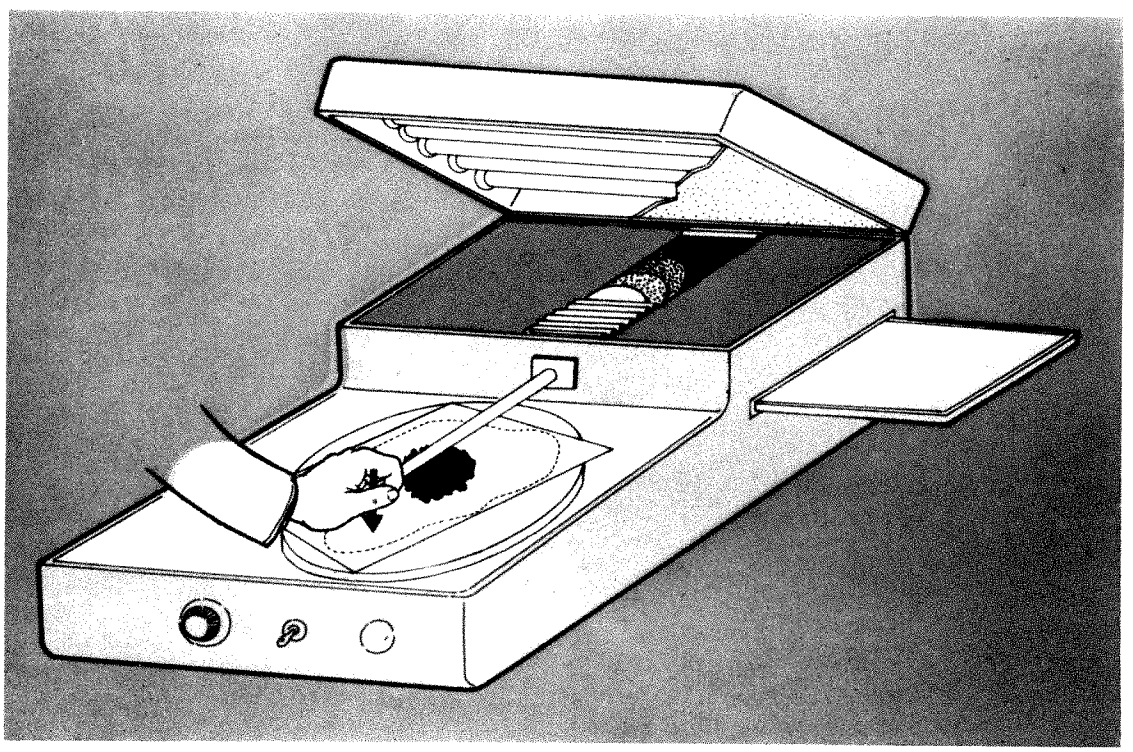


FIG. 8. The light isodensity planner is shown with a body cross-section on the turntable. The isodensity transparency is manually cammed to the body cross-section and lies between the light source in the cover and the unexposed film in the special cassette.

exposure can then be made. If the plan calls for a 90° crossed wedge field, the rotating turntable could be turned 90° also turning the enclosed turntable, and the slave arm is again positioned in contact with the skin surface before the second exposure is made. This would photographically simulate crossed wedge fields at the same source-skin distance (S.S.D.). Areas within the crossed fields would be represented by the double exposure. The cassette is then repositioned and the same isodose curve is exposed on a separate area, so that the calibration exposure is equal to the sum of the first and second exposures. This would produce a result (Fig. 9) similar to the example demonstrated in Figure 6. What has just been described for crossed wedge fields could be used for 3 or more fields or in the limit for partial or complete rotational problems. For rotational problems in which the source-skin-distance changes, the above system, which is based on S.S.D. curves, develops an increasing error as the contour deviates from the round. The principal contribution to this error arises because of the inverse square law. While using source-axis distance (S.A.D.) curves will decrease this error, a modification can be made when this error is considered too large by using an additional transparency which attenuates the light in proportion to the inverse square law. In these instances the unexposed film is exposed by a beam of light which must first pass through the compensating inverse square law transparency and then through the standard isodose transparency system.

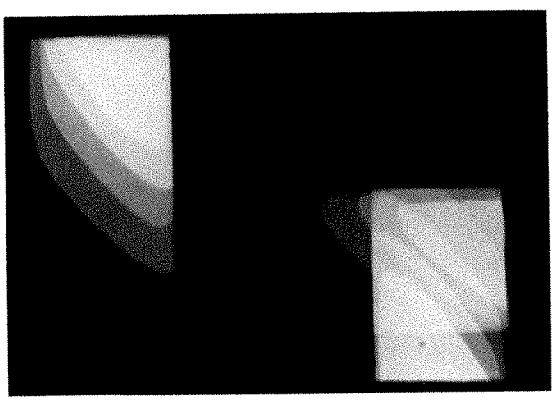


Fig. 9. An example of a crossed wedged field done on the light isodensity planner is shown. Within the region common to both fields the density can be converted to dosage from the adjacent calibration curve.

READOUT SYSTEMS

The simple manual method of field superposition requires no special readout system because the observer can determine the dose-density relationship by visual inspection. With the analog photographic system the film on which the multiple exposures are made must be evaluated by a density-dose analog converter. The calibration curve is first evaluated and then this density-dose relationship applied to the overlapped areas. The simplest form o density-dose analog converter is a densitometer. With it the calibration isodose curve is evaluated and the bands of grayness are measured in terms of specific density. Since the 100 per cent level is established by the given dose (for example 200 rads as illustrated in Fig. 6) then the density for the 80 per cent band representing a dose of 160 rads is determined. With this information the overlapped areas are examined with a densitometer. Any density value equal to the value obtained for the 80 per cent band on the calibration curve equals 160 rads. Similarly, a density can be compared to the calibration curve and converted to rads. Figure 10 shows such a solution with representative points determined in this manner. A more sophisticated development of this concept is the use of a film isodose contour plotter which is commerically available (Fig. 11).[1] The entire piece of film is inserted in a typewriter type film scanner, the maximum and minimum densities determined and 10 intermediate divisions created. The film is then optically scanned line by line. Areas of equal density are represented by 1 of 10 numerical symbols. A symbolic, digital analog is produced (Fig. 12*A*). The dose to any treated area can be determined by checking its symbol against the symbols in

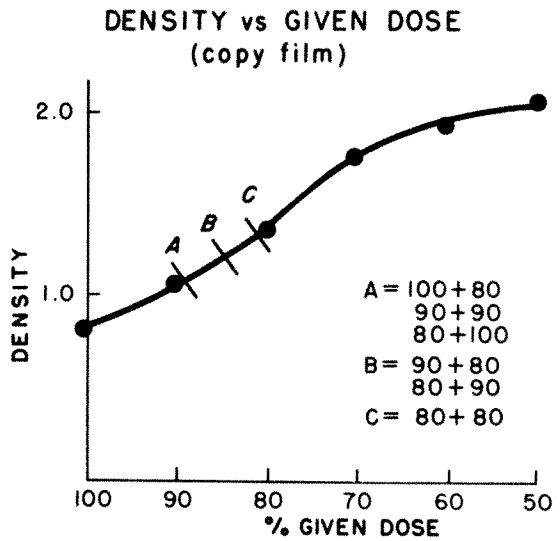
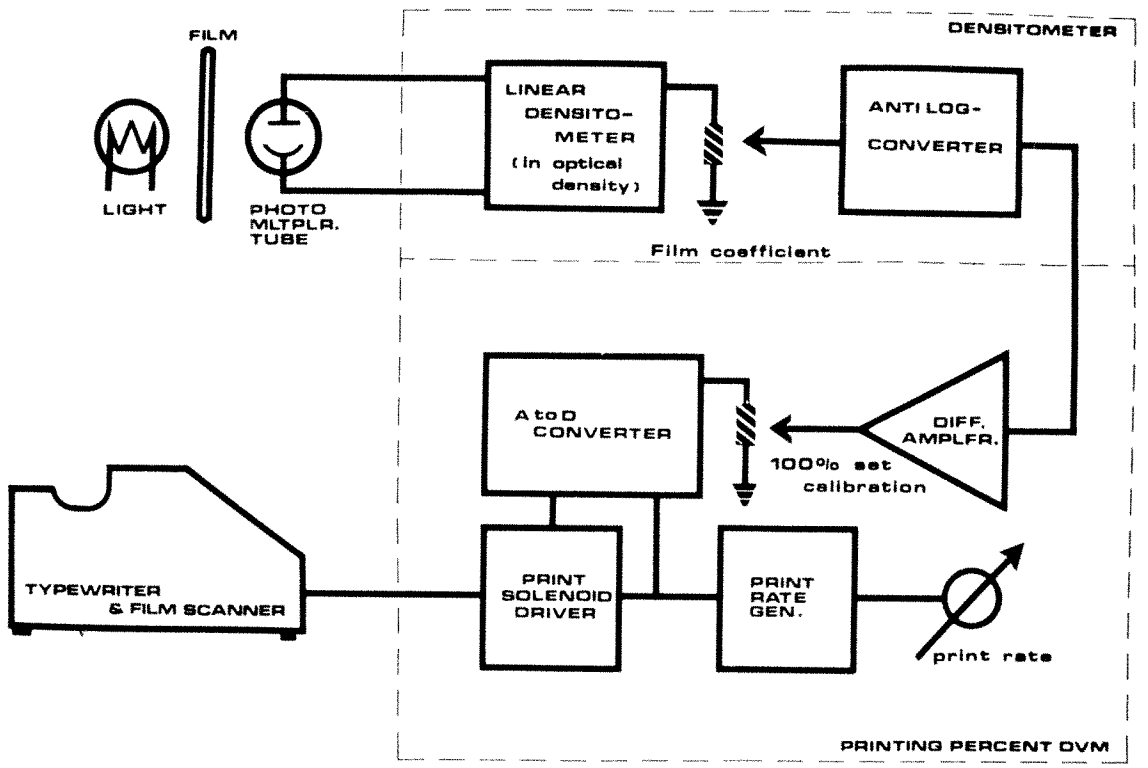


Fig. 10. Employing a densitometer the calibration curve of Figure 9 was used to determine the density-dose curve shown here. Points A, B, C in the double exposed crossed wedged field were measured with the densitometer and the results in rads were determined from the graph.

the calibration curve. Figure 12*B* is hand colored to better illustrate these areas. A more sophisticated instrument, also commercially available, uses a 4 color isodensitracer with even higher accuracy. It is particularly good for rotation problems in which the changing gray area is more subtle and continuous.[5] Another system of some-



FILM ISODOSE CONTOUR PLOTTER

Fig. 11. The results shown in Figure 10 were introduced into the typewriter film scanner. Maximum and minimum densities are determined and the range divided into 10 divisions. The entire film is then scanned and the density of each point is represented by a symbol from 0 to 9. This result is shown in Figure 12.

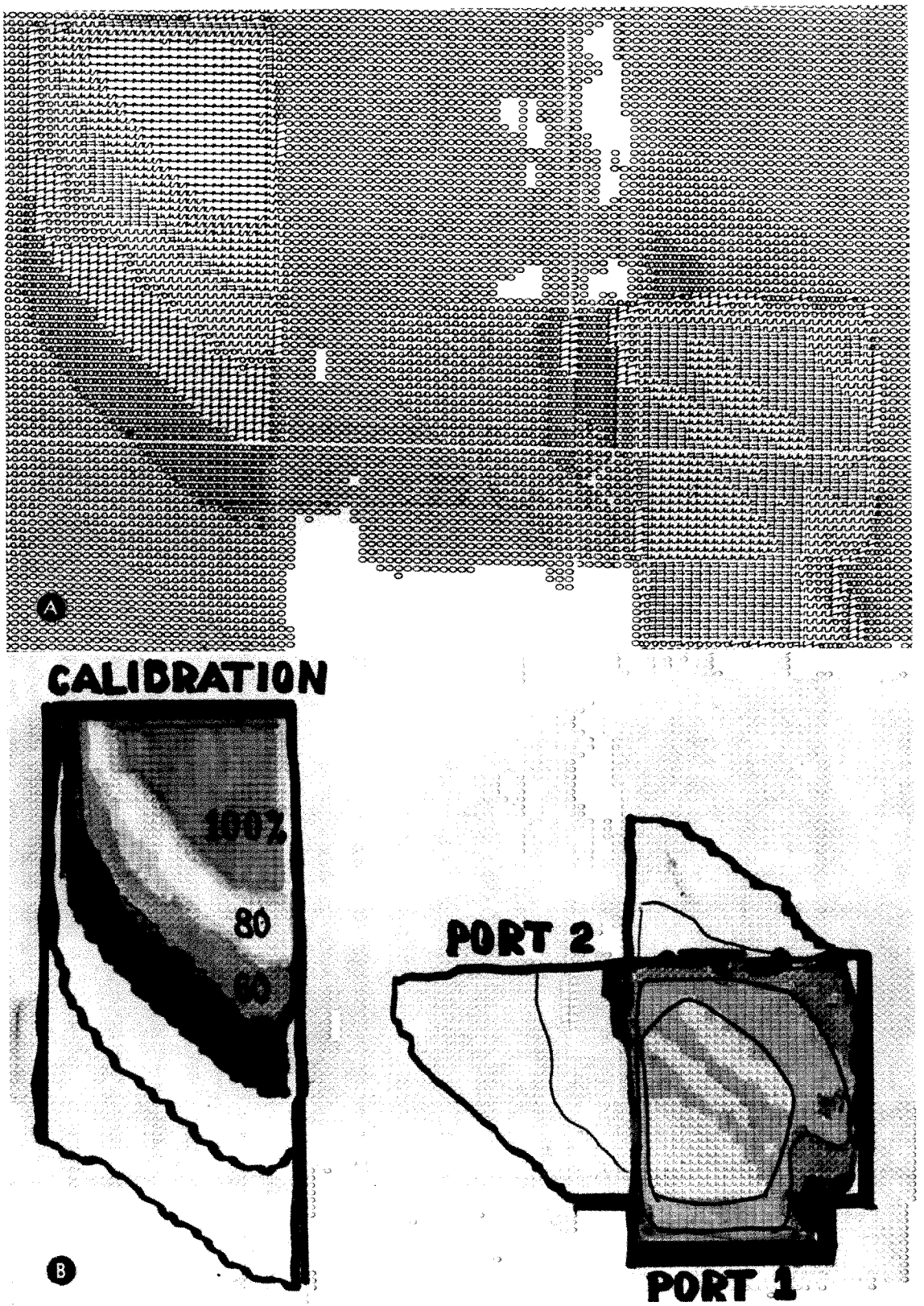


FIG. 12 (*A*) The original curve has been converted into a digital representation. (*B*) Numerically equivalent zones (areas of isodensity) were colored for clarity and appear as different shades of gray.

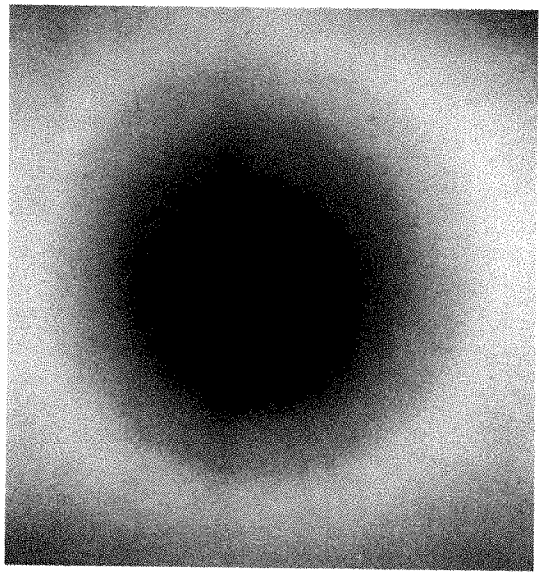


FIG. 13. This illustrates a rotation solution for a circular cross-section.

what lower accuracy, but with dramatic visual impact which would be helpful for teaching, is the use of a closed circuit color television system. A film placed on a viewbox is viewed with a color television camera; areas of uniform density are shown by a single color on the television screen and can be compared to the color representation of the calibration curve. Thus, the color television system acts as an analog density converter. More subtle changes in density can be evaluated with the same ease; Figure 13 illustrates a rotational solution for a round cross-section.

DISCUSSION

The system described is believed to offer many advantages over the present widely used hand calculated methods and can be provided at a cost substantially less than the computer oriented systems which are being developed today. Planning, using the isodose transparencies on a horizontal viewbox, should have widespread application. The use of a light isodensity planning unit would permit greater flexibility and permit solutions for even the most complicated problems.

ADVANTAGES

1. *Teaching aid.* The observation of changing isodensity patterns which simulate radiotherapy fields interacting should more quickly develop a concept of cause and effect in radiotherapy planning. This visual display should be helpful in the teaching and training of residents, physicists and technicians.

2. *Rapid solutions.* Multiple solutions can be evaluated by visual inspection in minutes and often in seconds. The final solution can be recorded on film, processed and be available for the chart as a permanent record in minutes.

3. *Accuracy.* Using the present isodose curves, isodose transparencies can be created with an accuracy of plus or minus 5 per cent. Greater accuracy can be achieved by using isodose curves with 5 per cent gradations. A uniform change in grayness from maximum to minimum could provide an accuracy of perhaps as low as plus or minus 2 per cent.

4. *Permanent record.* The photographic record produced by either system is a permanent record available for chart or folder. In addition to recording the shape of the field there is also a record of the dosage to each individual point.

5. *Inexpensive.* Transparencies could be mass produced at a relatively low cost and the unit proposed would be substantially less expensive than computer systems under development. Moreover, the saving in personnel time should be substantial and the additional accessories needed are commonly found in an existing radiotherapy department.

DISADVANTAGES

1. *Individual isodensity curves are required for each machine.* The need for different isodensity transparencies is exactly the same as the need for different isodose curves. Standardization by the principal manufacturers of cobalt 60 sources and collimation systems would make a set of standardized isodose transparencies possi-

ble. These standardizations are being made[10] and an analog set of isodose transparencies are being constructed.[2] Unusual systems, or special collimator designs, or S.S.D. variations causing significant changes in the isodose curves would require special isodose transparencies. This system can also be used for linear accelerators, other isotope sources or even electron beam equipment. All that is required is a set of representative isodose curves from which a light isodensity analog can be constructed.

2. *Inaccurate for curved surfaces.* Manipulation of the standard isodose curves can compensate for significantly curved surfaces in conventional planning. The proposed isodose transparencies assume a field perpendicular to a straight edge of the body. When the body curve is sufficient to cause an undesirable inaccuracy, a lead or wax compensator can be introduced between the source and the patient and thereby produce a perpendicular field.

3. S.S.D. *curves are inaccurate for rotation.* As the cross section deviates from a circle, the S.S.D. curves become increasingly more inaccurate because of the inverse square law. To some extent this inaccuracy could be reduced by creating S.A.D. curves. However, a more sophisticated and accurate solution would be to use a compensator transparency whose grayness varies proportionally with the inverse square law. By placing this between the light source and the isodose transparency based on a S.S.D. isodose curve, the transmitted light can be altered to compensate for the inverse square law inaccuracy.

COMMENT

It is believed that the basic system of isodose transparencies in which two fields weighted 1:1 are evaluated on a viewbox will have widespread application. The majority of radiotherapy cases commonly encountered can be rapidly managed with this method by unsophisticated personnel who can quickly be taught these new techniques. The results recorded on Polaroid film could then be rapidly checked by a more experienced planner and the final result used as a permanent record for the patient's chart. Those problems which cannot be solved by the visual inspection method can be solved with the light isodensity planning unit. It offers complete flexibility and can be used for even the most complicated solutions. The resulting films are self calibrated and are therefore independent of variations in film, exposure technique or development processing. The method is direct, simple, visual and accurate.

SUMMARY

A simplified radiotherapy planning system is proposed which is based on the conversion of the conventional isodose curves into film transparencies. These film analogs can be superimposed to visually portray radiation field interactions. More complicated solutions can be solved on a proposed light isodensity planner. This system will permit the solution of simple coplanar fields, multiple fields (including wedged and nonwedged fields), partial rotation or complete rotation or any combination of the above. It can be operated without special training and utilizes equipment usually found in a radiotherapy department. It is of special help to smaller therapy departments and private practices with limited personnel to document their planning. It will be very helpful in teaching centers where radiology residents, physicists and radiotherapy planners will find it a useful teaching aid.

Gerald S. Freedman, M.D.
Department of Radiology
Yale University School of Medicine
333 Cedar Street
New Haven, Connecticut 06510

We wish to thank Mr. A. Roestel of the Artronix Engineering Company, St. Louis, Missouri for his cooperation in producing film analog-digital conversions, and Mr. L. Whiting of Kodak Company and Mr.

Huber of Dupont Company for technical assistance with the many film problems.

REFERENCES

1. Artronix Engineering, 4390 Lindell Blvd., St. Louis, Mo.
2. FREEDMAN, G. S. To be published.
3. HASS, L. I. More rapid method of isodose analysis. *Radiology*, 1953, *61*, 222–235.
4. HOWARTH, J. L., and PICK, V. J. Use of new multi-field isodose contour plotter. *Brit. J. Radiol.*, 1960, *33*, 265–267.
5. Isodensity Tracer. Technical Operations Co., Mt. View, Calif.
6. Kodak Co. Tom Callear, personal communication.
7. Kodak Co. Neutral Density Attenuators, No. P-114.
8. Moos, W. S., and WEBSTER, E. W. Automatic tissue dose computer for use in supervoltage rotational therapy. *Radiology*, 1952, *59*, 729–736.
9. Moos, W. S., and SANDBERG, G. H. Photographic method for universal use in radiation isodose computation. Paper No. 56-24-2. University of Illinois, College of Medicine, Department of Radiology, Chicago.
10. Picker Corp. Personal communication.
11. POWERS, W. E., COX, D., GALLAGHER, I., GERTY, V. W., and HOLMES, W. F. Programmed Console for Radiation Therapy Planning. Scientific Exhibit of the Radiological Society of North America Meeting, 1966.
12. TSIEN, K. C., and ROBBINS, R. Photographic representation of isodose patterns by application of Sabattier effect. *Brit. J. Radiol.*, 1966, *39*, 1–6.
13. UNGER, E. M. Simplified method of studying volume dose distribution. *Brit. J. Radiol.*, 1943, *16*, 274–278.

Vol. 105, No. 3

RADIATION TOLERANCE OF THE THORACIC SPINAL CORD*

By THEODORE L. PHILLIPS, M.D., *and* FRANZ BUSCHKE, M.D.
SAN FRANCISCO, CALIFORNIA

SINCE radiation injury to the spinal cord results in severe and irreversible morbidity, its avoidance is often a major factor in planning treatment. Irradiation of the spinal cord has been the subject of many reports, and rough guidelines have been established as to its tolerance.[1–3] Most of the data have related to radiation tolerance of the cervical cord, however, and those regarding tolerance of the thoracic spinal cord are limited. This limitation probably results because few malignant tumors of the thorax were irradiated until recent years, and survival was short. Vaeth[9] reviewed the results of irradiated neoplasms treated at this hospital from 1957 to 1963. Only a few thoracic spinal cords had received radiation and in none had myelitis developed. Since techniques have changed and the number of long-term survivals have increased, a review of the more recent cases was deemed worthy.

MATERIAL AND METHOD

All patients treated between 1958 and 1966 for carcinoma of the lung, trachea, and esophagus, or for thymoma, were reviewed for the occurrence of myelitis. Lymphomas were not included in this review because of the smaller doses of radiation in these patients and since no permanent myelitis has been observed in such patients. The study was limited to those patients in whom myelitis had developed and to those living longer than 18 months without myelitis. A survival of at least 18 months was believed necessary to exclude myelitis. The treatment records established that irradiation had included the spinal cord and that the subsequent myelitis was not caused by tumor or trauma. Doses delivered to the spinal cord at the upper, middle, and lower end of the fields were calculated in rads. Isodose curves and lateral roentgenograms were used to correct for magnification and changes in contour. The maximum doses to the spinal cord were related to the number of fractions and to the over-all time in the subsequent analysis.

RESULTS

A total of 350 patients was treated for nonlymphomatous malignant tumor in the chest between 1959 and 1966. These tumors included 248 lung carcinomas, 7 tracheal carcinomas, 72 esophageal carcinomas, and 23 thymic tumors. Definite severe and progressive signs of myelitis developed in 3 patients of this group in 10 to 13 months after treatment (Table 1). In an additional 37 patients, who survived 18 to 78 months, no signs of myelitis were noted.

The patients either with or without myelitis had had 5 to 10 segments of spinal cord irradiated. Cobalt 60 or 1 mev. radiation had been used in all cases and the plans of treatment were similar. Treatment was directed through opposing fields or an occasional single field, averaging 15×10 cm.

The major differences between those in whom myelitis developed and those without symptoms were in the areas of dose, time, and number of fractions. The calculated maximum doses to the spinal cord were plotted against over-all time (Fig. 1) and against the number of fractions (Fig. 2). Lines were drawn through the lowest points representing patients with myelitis. Most of the uninvolved cases fell below the line when over-all time *versus* dose was

* Presented at the Fiftieth Annual Meeting of the American Radium Society, Miami Beach, Florida, April 7–11, 1968.
From the Department of Radiology, Section of Therapeutic Radiology, University of California School of Medicine, San Francisco, California.
This investigation was supported in part by NIH Training Grant No. TI-CA 5177.

TABLE I

RADIATION MYELITIS OF THE THORACIC SPINAL CORD IN IRRADIATED PATIENTS

Case No.	Radiation Energy	Maximum Dose to Cord (rads)	Time in Days	Number of Fractions	Segments Irradiated	Interval to Myelitis	Vertebral Level of Myelitis	Total Observation Time
I	Co^{60}	3,300	23	6	T_1 to T_6	11 months	T_3	36 months; alive
II	Co^{60}	4,350	24	6	T_6 to T_{11}	13 months	T_{10}	16 months; dead
III	1 mev.	7,000	61	26	T_3 to T_{11}	10 months	T_6	13 months; dead

plotted, but all were below when number of fractions *versus* dose were plotted. The number of fractions or size of single increment may be more important than the over-all time. To evaluate both of these factors, the doses were also reduced to nominal single doses (NSD) according to the tables of Ellis.[4] These tables take into account both the number of fractions and the over-all time (Table II). The NSD appeared to relate fairly well to the amount of radiation injury. Myelitis developed in 1 of 12 patients with values of NSD between 1,500 and 1,750, and in 2 of 4 with values between 1,750 and 2,000 rets (rads equivalent therapeutic). The 3 patients in whom myelitis developed are described.

REPORT OF CASES

CASE 1. This 78 year old woman appeared in February 1965 with an anaplastic carcinoma of the right bronchus. A peripheral adenocarcinoma had been excised from the same lung in 1959 by lobectomy. A bronchoscopy and biopsy were done of a 5×4 cm. mass which was lateral to the hilum. A single 10×8 cm. field, centered 2.5 cm. inferior and 1 cm. to the right of the sternal notch was irradiated. A maximum entrance dose of 5,800 rads was given in 6 fractions over a period of 23 days using Co^{60} teletherapy. The fractions were not evenly spaced, but were given as 2 groups of 3 daily treatments. Despite the use of an anterior field, the upper thoracic spinal cord received 3,300 rads from this treatment course (NSD = 1,525 rets). This dose resulted because of the high location of the field and the marked narrowing of the patient's diameter at this level. A roentgenogram of the chest in November 1965, revealed radiation fibrosis of the right upper lobe. In mid-January of 1966, a sudden paralysis developed in both legs. The patient was admitted to San Francisco General Hospital where myelograms gave no evidence of abnormality. Muscle wasting and decubital ulcers were present and these progressed over the next 6 months. Reflexes were absent in the legs. Plantar stimulation caused marked withdrawal response. Analgesia was present to the level of the third thoracic dermatome. Vibratory and proprioceptive senses were impaired but not absent in the lower extremities. There was loss of bladder and bowel control. The patient was subsequently referred to a nursing home. She is still alive, 2 years after myelitis developed, but is in poor condition.

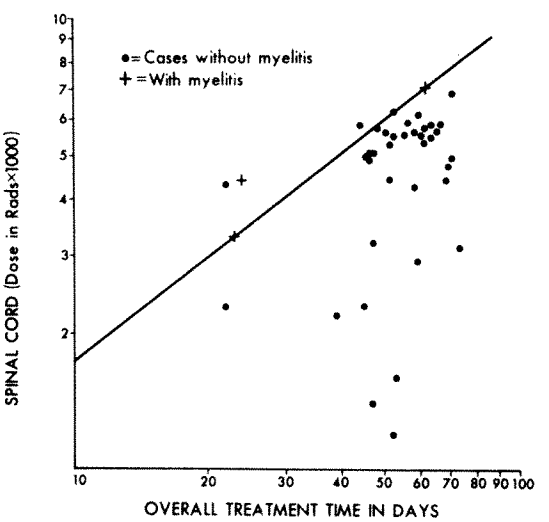


FIG. 1. Log-log plot of maximum radiation dose to thoracic spinal cord *versus* over-all treatment time in days. Crosses denote patients with myelitis. Line drawn for reference through lowest dose yielding myelitis has a slope of 0.75.

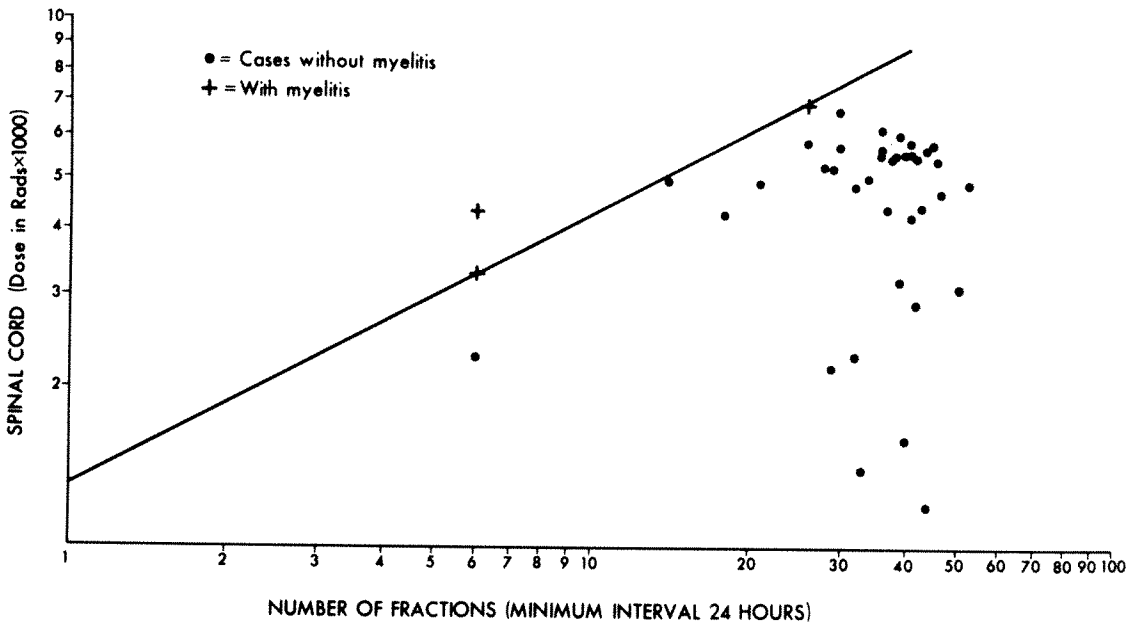


FIG. 2. Log-log plot of maximum radiation dose to thoracic spinal cord *versus* number of treatment fractions. Line drawn through lowest dose yielding myelitis has a slope of 0.5. Crosses denote patients with myelitis. All fractions were spaced at least 24 hours.

CASE II. This 54 year old man was first seen in April 1965 because of chest pain, cough, and a 10 cm. right hilar mass. Thoracotomy revealed a large anaplastic carcinoma infiltrating the right upper and lower lobes with metastasis to the mediastinal lymph nodes. Resection was not attempted and the patient was referred for radiation therapy. A single posterior 12×11 cm. field was centered 4.5 cm. to the right of the midline and extended from the sixth to the eleventh thoracic vertebra. With Co^{60} tele-

TABLE II

RELATIONSHIP BETWEEN NSD* AND MYELITIS OF THORACIC SPINAL CORD—UNIVERSITY OF CALIFORNIA PATIENTS

NSD Dose Range (rets†)	Number with Myelitis
<1,000	0/8
1,000 to 1,250	0/6
1,250 to 1,500	0/10
1,500 to 1,750	1/12
1,750 to 2,000	2/4
Total	3/40

* Nominal single dose.
† Rads equivalent therapeutic.

therapy, a maximum entrance dose of 5,800 rads was given in 6 fractions in 2 groups of 3, over 24 days. The spinal cord received a dose of 4,350 rads (NSD = 1,990 rets). Excellent regression of the mass was effected and the patient gained weight. In June 1966, sudden leg weakness developed as well as urinary retention, fecal incontinence, and numbness of the lower abdomen and legs. Within a few days the patient was completely paralyzed and a sensory loss below the first lumbar vertebra and a partial anesthesia as high as the ninth thoracic vertebra were noted. At this time the patient was admitted to another hospital where the previous course of radiation therapy was not fully appreciated. A myelogram was reported as normal, but local radiation therapy was given to the level of the lesion (1,500 r skin dose) without response. The neurologic state remained unchanged after this treatment until September 1966 when, after a sudden bowel obstruction, the patient died. At necropsy tumor involved the right hilar area, the liver, the adrenals, the kidneys, and the jejunum. The jejunal lesion had perforated and caused death. No metastasis to the central nervous system was found.

The spinal cord was studied in detail at the University of California Medical Center by Dr.

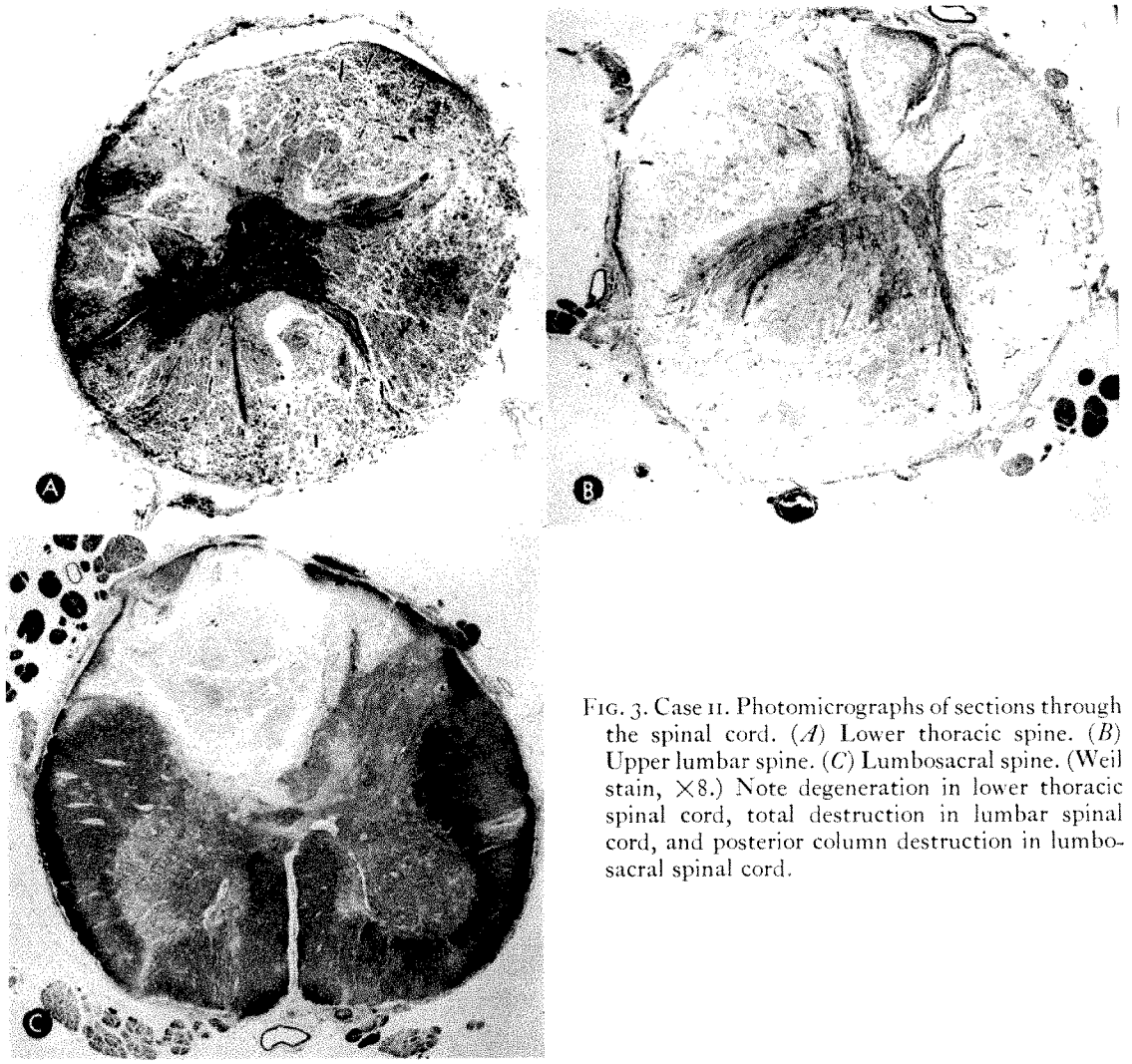


FIG. 3. Case II. Photomicrographs of sections through the spinal cord. (*A*) Lower thoracic spine. (*B*) Upper lumbar spine. (*C*) Lumbosacral spine. (Weil stain, ×8.) Note degeneration in lower thoracic spinal cord, total destruction in lumbar spinal cord, and posterior column destruction in lumbosacral spinal cord.

John Lee and Dr. Nathan Malamud. Grossly and histologically the lumbar spinal cord (lower thoracic vertebral level) was necrotic. Sections revealed necrotizing myelopathy extending from the lower thoracic to the lumbosacral cord elements, corresponding well with the actual level of irradiation (Fig. 3, *A*, *B* and *C*). Wallerian degeneration of the ascending tracts was noted above the involved area and in the pyramidal tracts. The lesion itself consisted of unsystematized homogeneous necrosis of the white matter with poor glial reaction, sparse gitter cells and no inflammation. The posterior columns were affected at the upper and lower margins of the lesion, but the entire spinal cord was necrotic at the center of the lesion, including the gray matter. Vascular changes were minimal and no tumor was seen in the cord or adjacent vertebrae. The lesion was considered representative of radiation myelitis.

CASE III. In this 35 year old man a right hilar mass was causing symptoms of dyspnea, chest pain, and weight loss in May 1963. Thoracotomy revealed a poorly differentiated squamous cell carcinoma adherent to the right pulmonary artery. The lesion was not resectable and preoperative irradiation was attempted. Opposing fields 16×11 cm., centered 2 cm. to the right of the midline and extending from the third to the eleventh thoracic vertebra received radiation with 1 mev. energy. Because of skin reaction anteriorly, the posterior field received an entrance dose of 6,900 rads and the

anterior field 5,450 rads. The maximum dose to the spinal cord was 7,000 rads in 26 fractions over 61 days (NSD = 1,970 rets). The patient was treated only 3 times per week and allowed an interval of 8 days of rest because of the skin reaction.

Pneumonectomy was performed on August 12, 1963 at the Veterans Administration Hospital in San Francisco. A tumor was resected, which contained viable cells, but which did not involve the surgical margins or lymph nodes. In May 1964, 10 months after completion of therapy, weakness and a sensory loss developed. These became complete after 2 weeks and extended to the mid-dorsal level. The patient was admitted to the Veterans Administration Hospital in Spokane, Washington. Initially, reflexes were hyperactive. Two myelograms were reported as normal, as was the cerebrospinal fluid. Prednisone was started but elicited no response. The patient died in August 1964. Permission for necropsy could not be obtained.

DISCUSSION

More aggressive treatment schemes and combined radiation and surgical therapy of thoracic neoplasms have increased the number of survivors beyond 18 months after treatment. Such survival and the higher doses of recent years have increased the risk of radiation myelitis. In 1965, Vaeth[9] reviewed 79 patients, including those with lymphomas, with thoracic irradiation, of whom 19 survived more than 16 months after irradiation. In none of these did myelitis develop. The present review yielded 350 patients of whom 38 survived more than 18 months and 3 in whom a severe radiation myelitis developed. These results represent an incidence of about 1 per cent of the treated patients and 8 per cent of long-term survivors.

Recently Reagan *et al.*[8] described 4 basic types of radiation myelitis: (a) the initial transient type characterized by Lhermitte's sign and eventual return to normal; (b) the rare degeneration of the lower motor neuron seen in some patients irradiated to the abdomen; (c) acute and complete quadriplegia or paraplegia developing over a few days; and (d) chronic progressive myelopathy developing over weeks and months, and involving mainly the lateral columns. Our Case 1 appears to fall into the latter group in that changes were progressive and a complete transverse myelitis did not develop. In Cases II and III sudden and complete paraplegia developed; these cases appear to fall into the third group. Necropsy confirmation was available for Case II and complete destruction of the cord was evident at the middle of the treated area.

Analysis of the time-dose relationships for these patients reveals that such complications as myelitis are probably avoidable. Although in the initial analysis of Boden,[2] a limit of 3,500 r in 17 days for large fields was predicted, a projection on the basis of Strandqvist's curves of 4,200 r in 6 weeks is obviously too low. The limit of 3,300 r in 42 days set by Pallis *et al.*[7] also seems too low, since we have treated many patients to much higher doses without sequelae. *The limit of tolerance appears to increase with time and fraction numbers more rapidly than Strandqvist's curves for skin tolerance.* The slope for skin tolerance derived by Strandqvist was 0.33 based on over-all time. The line drawn through the myelitis cases receiving the lowest doses in this series gives a slope of 0.5 for the number of fractions and 0.75 for over-all time.

On this basis at least, and considering the small number of cases, tolerance appears to be low for small numbers of fractions but increases rapidly as their number rises. The incidence of myelitis as noted by Locksmith and Powers[6] was 12.5 per cent in patients treated to 4,000 rads in an average of 15 fractions over 3 weeks. Lampe[5] observed this to be the case with brain necrosis, noting late damage after 2,500 r in 6 to 8 days. Thus, tolerance is low for short times of treatment and few fractions. The number of fractions and, correspondingly, the size of the single doses may be more important than the over-all time, at least on the basis of the few cases reported.

By combining 3 of the cases of radiation injury of the thoracic spinal cord reported by Atkins and Tretter[1] (Cases VIII, XII, and

TABLE III

RELATIONSHIP BETWEEN NSD AND MYELITIS OF THORACIC SPINAL CORD—COMBINED CASES*

NSD† Dose Range (rets‡)	Number with Myelitis
<1,000	0/8
1,000 to 1,250	0/6
1,250 to 1,500	2/12
1,500 to 1,750	8/19
1,750 to 2,000	2/4
Total	12/49

* Includes patients reported by Atkins and Tretter,[1] Locksmith and Powers,[6] and our patients.
† Nominal single dose.
‡ Rads equivalent therapeutic.

XIII), those of Locksmith and Powers,[6] and our cases, dose *versus* number of fractions was plotted. The data derived show that a line connecting 6,000 rads in 35 fractions (7 weeks) and 5,000 rads in 25 fractions (5 weeks) would exclude all myelitis cases. Thus, such doses would be tolerated if given in increments of 200 rads or less. Short courses or a few large fractions appear to be dangerous. From this plot, 1,300 rads in 2 fractions and 3,000 rads in 10 fractions would appear to be the safe limit. When the data of Atkins and Tretter[1] and of Locksmith and Powers[6] are converted to NSD values (Table III), the limit would appear to be 1,500 rets (rads equivalent therapeutic) with only 2 cases occurring below this level. Although the NSD value is lower than predicted by the plot of dose *versus* number of fractions for larger fraction numbers, it appears to be a useful and safe index, particularly in evaluating wide variations from the normal patterns.

SUMMARY

Three instances of radiation myelitis of the thoracic spinal cord were found among 350 patients treated for carcinoma of the lung, esophagus, and trachea, or for thymic tumors, 40 of whom survived more than 18 months. These 3 patients and the 37 additional patients surviving more than 18 months after irradiation were studied in detail.

The time-dose relationships were reviewed and analyzed as a function of number of fractions and of over-all treatment time. The results suggest that the number of fractions is the most important factor in the determination of late radiation damage to the spinal cord.

We conclude that radiation myelitis can probably be prevented by avoiding an excessive total dose to the spinal cord and by planning treatment that does not deliver more than 200 rads per fraction.

Theodore L. Phillips, M.D.
Department of Radiology
University of California
San Francisco Medical Center
San Francisco, California 94122

REFERENCES

1. Atkins, H. L., and Tretter, P. Radiation myelopathy: time dose considerations. *Acta radiol.* (Ther.), 1966, *5*, 79–92.
2. Boden, G. Radiation myelitis of cervical spinal cord. *Brit. J. Radiol.*, 1948, *21*, 464–469.
3. Dynes, J. B., and Smedal, M. I. Radiation myelitis. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1960, *83*, 78–87.
4. Ellis, F. Relationship of biological effect to dose-time-fractionation factors in radiotherapy. In: Current Topics in Radiation Research. Volume IV. Edited by M. Ebert and A. Howard. North-Holland Publishing Company, Amsterdam, 1968, pp. 357–397.
5. Lampe, I. Radiation tolerance of central nervous system. In: Progress in Radiation Therapy. Volume I. Edited by F. Buschke. Grune & Stratton, Inc., New York, 1958, pp. 224–236.
6. Locksmith, J. P., and Powers, W. E. Permanent radiation myelopathy. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1968, *102*, 916–926.
7. Pallis, C. A., Louis, S., and Morgan, R. L. Radiation myelopathy. *Brain*, 1961, *84*, 460–479.
8. Reagan, T. J., Thomas, J. E., and Colby, M. Y., Jr. Chronic progressive radiation myelopathy: its clinical aspects and differential diagnosis. *J.A.M.A.*, 1968, *203*, 106–110.
9. Vaeth, J. M. Radiation induced myelitis. In: Progress in Radiation Therapy. Volume III. Edited by F. Buschke. Grune & Stratton, Inc., New York, 1965, pp. 16–26.

CHANGING PERSPECTIVES IN OXYGEN BREATHING AND RADIATION THERAPY*

By PHILIP RUBIN, M.D., COLIN A. POULTER, M.B., B.S., *and* RAYMOND S. QUICK, B.Sc.
ROCHESTER, NEW YORK

THE central issue in regard to oxygen breathing and radiation therapy is whether the proportion of anoxic cells *decreases or increases* during a fractionated course of irradiation. The radiobiologic evidence suggests strongly that the anoxic population of cells is gradually oxygenated due to a decrease in intercapillary distance and improved circulation which occurs after the absorption of the irradiated dead oxygenated cells, thereby increasing the availability of oxygen to reach the hypoxic cell fraction. This phenomenon has been referred to as "reoxygenation."

1. The "supervascularization effect" of irradiated regressing tumors[27,29] has been confirmed by Reinhold[26] who employed fluorescent microscopic techniques to identify vascular patterns. He noted that, following exposure to fractional irradiation, portions of tumors showed an increase in the density of the capillary network. In human cervical cancer, Bergsjo,[2] employing colpophotographic studies in 143 cases, showed the improvement of the fine circulation with tumor regression and concluded, "Altogether, the observations fit the idea of a progressive increase in oxygenation during the early phase of fractionated radiotherapy."

2. Direct probing of regressing tumors also correlated the supervascularization effect with increased oxygen tension in the tumor, particularly under conditions of oxygen breathing at 1 atmosphere.[6,13,28] Kolstad and Bergsjo[19] indicated that if multiple readings were taken of an irradiated regressing cervical cancer, the oxygenation values would also show an increase.

3. The conversion of the anoxic fraction of the cell population to oxygenation can be distinguished in two experimental systems using transplantable tumors in mice. In DBA mice with mammary cancer, the anoxia to air ratio for TCD_{50} (tumor cure dose of 50 per cent in 120 days) was 1.08 for single doses and 1.53 for fractionated doses.[31] In another study, van Putten and Kallman[38] demonstrated the constancy of the percentage of anoxic cells. A transplantable sarcoma in C_3H mice was given 5 daily doses of 200 r and, after cessation of irradiation, the TCD_{50} curves were obtained with test doses in living air-breathing mice and in nitrogen-asphyxiated dead mice. The important finding is that two curves with similar slopes were found after fractionated irradiation as compared to before treatment. If only the oxygenated cells were destroyed by fractional irradiation during air breathing, the tumor would be essentially anoxic (80 to 90 per cent). Computing the S_{alive}/S_{dead}, only 19 to 20 per cent of the tumor cells are anoxic in air breathing. Both studies are compatible with the view that fractional irradiation reduces intercapillary distance and improves circulation and that anoxic cells before a given radiation exposure have a high probability of being oxygenated afterwards.

The theoretic scheme of events is portrayed by Fowler,[15] using a computer program which determines surviving fractions of viable cells and specifies the shape of survival curves, oxygen enhancement ratio and initial proportion of anoxic cells (Fig. 1). The major assumption in predicting the success or failure of radiotherapy is

* Presented at the Fiftieth Annual Meeting of the American Radium Society, Miami Beach, Florida, April 7–11, 1968.
From the Department of Radiation Therapy, University of Rochester School of Medicine and Dentistry, Strong Memorial Hospital, Rochester, New York.
This work was supported in part by U. S. Public Service Grant #CA-05102-07.

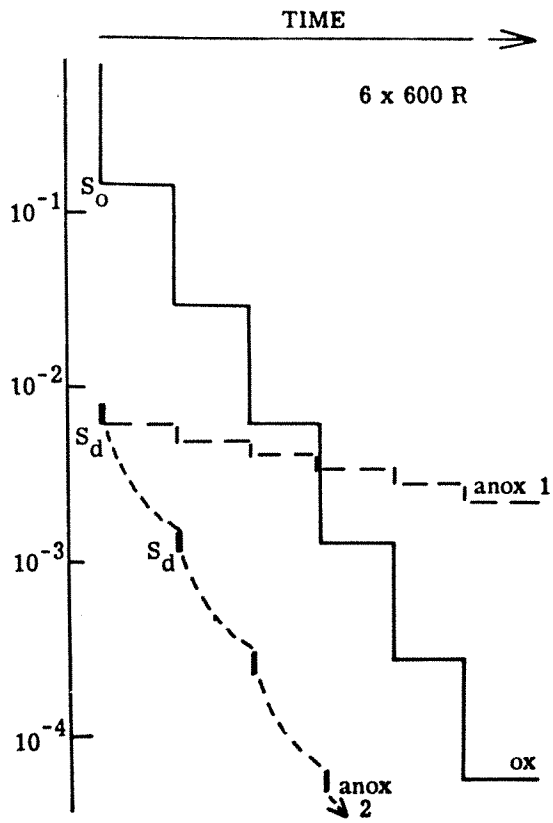


FIG. 1. *Calculations of surviving fractions of viable cells based on a computer program.* Results of computer program shown graphically. Each dose of 600 r reduces the surviving fraction of oxygenated cells to S_0 and anoxic cells to S_d. No repopulation is assumed here. If none of the anoxic cells become oxygenated as the treatment proceeds, the curve *anox 1* is obtained. If, however, some anoxic cells become oxygenated between successive fractions, so that the proportion of anoxic cells is kept about 10^{-2} of the surviving aerobic cells, then the curve *anox 2* is obtained, and the anoxic cells *never* become predominant. Practical cases will lie between these extremes. (From, J. F. Fowler: Biological Foundations of Radiotherapy. Proceedings of the 11th International Congress of Radiology, Rome, 1965. Excerpta Medica International Congress Series No. 105, 1966.)

based upon whether the anoxic fraction of cells remains anoxic (Anox 1) or becomes oxygenated (Anox 2).

I. TUMOR CORD MODEL

The first Thomlinson and Gray model of a tumor cord[35] has been supplanted by Thomlinson currently[34] as a three dimensional rendering of the tumor cord and its microcirculation. The initial model devoid of capillaries indicated a zone of viable tissue and a necrotic core which increased in size as the cord increased in diameter. The oxygenation of tumor cells was presented as a function of distance from the capillary and oxygen diffusion. In 1960, Thomlinson[33] offered a diagrammatic map of a tumor section illustrating zones of "old" and "recent" necrosis and suggesting a dynamic system. The new model (1968) presents this more dynamic picture so that alterations in capillary distance, capillary length, blood flow, blood pressure, oxygen tension in plasma, oxygen diffusion and utilization in tissue and tissue hypoxia can be related spatially and physiologically.

Oxygen tension in capillaries falls along their length from about 100 mm. Hg at the arterial end to approximately 40 mm. Hg, the value in mixed venous blood. The fall results from the diffusion of oxygen in all directions from each point in the capillary wall in proportion to the gradient and is governed principally by the geometric arrangement of the capillaries, the oxygen tension at each point of their length and the rate of oxygen consumption of the tissue (Fig. 2, *A*, *B* and *C*). Fifty per cent of the increase in radiosensitivity of cells that is dependent on oxygen is reached at a tension of about 4 mm. Hg, and 90 per cent at 20 mm. Hg.

The variations introduced in the basic model include an increase in capillary length, and decrease in blood flow, parallel flow or contraflow in adjacent capillary.[30] The important factor to recognize is the effect on tissue oxygen tensions with changing circumstances. The use of hyperbaric oxygen breathing will not overcome the effects of focal compression and ectasia of vessels, sluggish circulation and capillary spacing. Coupling hyperbaric oxygen (HPO) with large fractional doses may further disrupt the microcirculation and worsen tumor and tissue oxygen tension. The selective regression of the parenchymal tumor compartment with decreased inter-

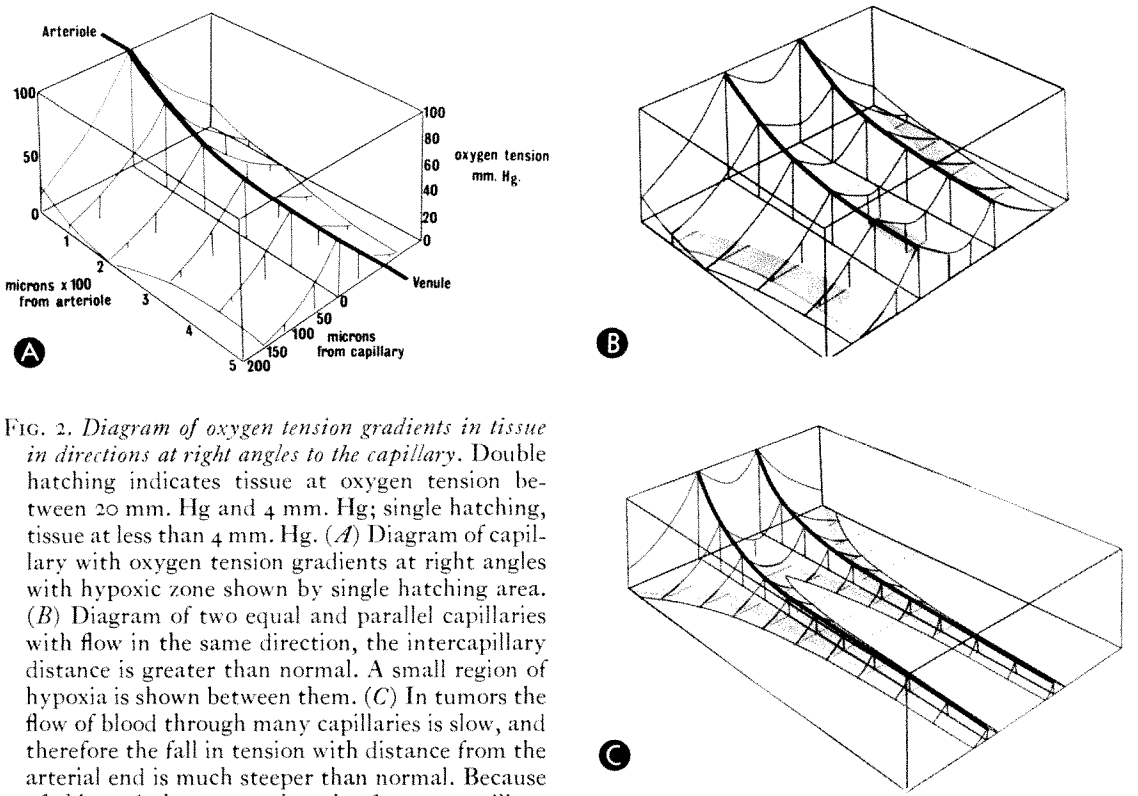


Fig. 2. *Diagram of oxygen tension gradients in tissue in directions at right angles to the capillary.* Double hatching indicates tissue at oxygen tension between 20 mm. Hg and 4 mm. Hg; single hatching, tissue at less than 4 mm. Hg. (*A*) Diagram of capillary with oxygen tension gradients at right angles with hypoxic zone shown by single hatching area. (*B*) Diagram of two equal and parallel capillaries with flow in the same direction, the intercapillary distance is greater than normal. A small region of hypoxia is shown between them. (*C*) In tumors the flow of blood through many capillaries is slow, and therefore the fall in tension with distance from the arterial end is much steeper than normal. Because of this and the greater length of many capillary pathways, extensive regions of hypoxia may develop between capillaries. With regression of a tumor, intercapillary distance decreases, blood flow increases and capillary length decreases all of which reverse unfavorable pathophysiologic factors and aid in increasing the oxygen tension of tumor tissue. (Courtesy of Dr. R. H. Thomlinson.)

capillary distance and shortening of capillary length may offer a better distribution of tumor oxygen tension than can be achieved by forcing the oxygen in at higher pressures. In fact, this has been shown by Suit *et al.*[31] in that the full oxygenation (2 to 3×) is not achieved in larger tumors (greater than 1.0 cm.).

The changing perspective in tumor cord model is a dynamic physiologic view of many variables which affect tumor oxygen tension. HPO is one possible approach and not particularly efficient as a means of effectively reaching all hypoxic cells. The search for physiologic means to increase blood flow needs emphasis coupled with a greater recognition of the pathologic and physiologic changes which occur with different fractionation schedules in a variety of tumors.

II. ANIMAL TUMOR EXPERIMENTS

The experimental work in animals indicating that atmospheric (100 per cent) oxygen breathing enhances radiation effect is often overlooked. In the first report of Gray *et al.*[16] detailed tabulations showed that a group of tumors irradiated with 1,000 r while the animals were breathing a 1 atmosphere of oxygen responded as well as the group given 1,500 r while the animals breathed air. There was a 50 per cent gain in radiation effect. Breathing 3 atmospheres of oxygen only enhanced the effect to the level seen with 2,000 r with air breathing, or another 50 per cent. More recently, Du Sault, Eyler and Dobben[11] indicated that atmospheric oxygen breathing augmented two different fractional schemes of treating spontaneous mammary adenocarcinomas in a C_3H strain of mice. This

augmentation ranged from 25 to 50 per cent greater tumor control as compared to base line values.

This approach was further explored by Inch *et al.*[17] who used C_3H isoimplants and C_3HBA isotransplants of a spontaneous mammary cancer. Irradiation was given to a tumor dose of 4,000 r in two divided exposures in 4 days to mice breathing air, 100 per cent oxygen, and 95 per cent oxygen and 5 per cent carbon dioxide. More improvement with 100 per cent oxygen breathing than with air breathing was noted in both types of implanted tumors. The breathing of 95 per cent O_2 and 5 per cent CO_2 augmented the survival rate only in the isoimplant tumors, since they are more hemorrhagic and necrotic compared with the isotransplant tumors, which are more vascularized. Of interest are the physiologic measurements during the different types of breathing. Pure oxygen at atmospheric pressure did not affect blood flow or heart rate, decrease respiration, or increase body temperature. The addition of 5 per cent CO_2 increased blood flow and respiratory rate, whereas the body temperature and heart rate were decreased. Curiously, Du Sault and associates[11] obtained a greater systemic reaction with the mixture of gases. The pursuit of this problem with polarographic methods using microelectrodes in tumors and normal tissues would be worth while in ensuring the maintenance of the best differential effect between the tumor and normal surrounding tissues. Subsequent studies by Du Sault[10] have indicated the value of adding 5 per cent carbon dioxide to atmospheric oxygen. Breathing this mixture has produced a further gain in cure rate in this animal tumor system owing to the resultant respiratory stimulation and vasodilatation, which cause more blood and, therefore, more oxygen to be carried to the tumor.

III. REOXYGENATION AND FRACTIONATION

The gain won through the use of high compression systems to increase the oxygenation of tumors may be offset by the decrease in fractionation. The greater the fractional dose, the more likely the occurrence of injury to the capillary bed of both neoplasms and normal tissue. Injury to the vascular bed of the tumor will reverse the trend toward a higher tumor oxygen level and increased radioresistance. Injury to normal capillaries will further alter the therapeutic ratio unfavorably.

Herein lies the dilemma of hyperbaric oxygen breathing. The oxygen enhancement ratio is best served by large fractional doses. The differential destruction of cells (aerobic *vs.* anoxic) occurs on the slope not on the shoulder of cell survival curves. Regular daily fractions of 150–200 r are essentially treating on the shoulder of the curve and have been advanced as a means of more efficiently killing anoxic cells.[1] Since there is little *in vitro* advantage to this approach, it is not surprising that no clinical study has shown this combination of HPO and small daily doses to be of much value.[4,18] The use of doses larger than 200 r, in the range of 500 r to 700 r, is an effective dose to take advantage of the oxygen enhancement ratio in an *in vitro* system.[37] *In vivo*, capillary damage will occur and increase with repeated large fractional doses, so that tumor anoxia could increase as well as increasing normal tissue damage. The therapeutic gain has not been great with HPO due to the increasing necrosis rate with increasing cure rates.

IV. CLINICAL EXPERIENCE

A. PRESENT SERIES

Since 1964, the policy of our department has been to explore the value of atmospheric oxygen breathing by mask in conjunction with radiotherapy. The only provision in placing a patient in the program was to have an observable mass by clinical examination or roentgenographic procedure. A large variety of patients (300) with cancer of the head and neck, breast cancer, cervical cancer, cancer of the lung and other miscellaneous groups have been so treated.

This report will be limited to our experience with head and neck cancer because this is the best target group for study. It represents a variety of patients, but all had squamous cell cancers that could be serially observed in their response and compared with normal tissue reactions. Although the series is not large, it indicates the potential value of oxygen breathing, since this group would have been placed into a HPO study.

All patients with primary squamous cell carcinoma of the nasopharynx, paranasal sinuses, oral cavity, oropharynx and laryngopharynx excluding lip were included from April, 1964, to December, 1967 (Table I). Lesions of the intrinsic larynx (T_1,T_2) were not included, nor were other T_1 lesions of the other sites in the first 2 years of the study. Patients treated solely by implants, moulds or peroral cones often fell into this category and were not suitable for oxygen breathing by mask. Of the 47 patients who started in the series, 3 recurrences after surgery and 2 patients with lesions later shown to be metastases from bronchogenic carcinoma were excluded. One patient did not have more than 2 weeks of irradiation and he too was not included. Of the 41 remaining patients, 8 have been followed less than 1 year, leaving 33 available for analysis with primary cancers of the head and neck. The majority were T_3, T_4 lesions and comprised 26/33 or 77 per cent of the group.

Of 33 patients treated, there is a 52 per cent survival rate from 1 to 4 years and a 67 per cent control rate, in that intercurrent deaths by chance reduced the survival results (Table II) to a significant degree. Of the 5 patients listed as dead without disease, all were autopsy proven. Deaths were due to auto accident in 3 cases, 1 to rheumatic heart disease and 1 to chronic pulmonary disease. The cumulative survival curves demonstrate a survival rate of 85 per cent to 72 per cent at 1 and 4 years (Fig. 3).

The major achievement has been the high measure of local control of primary lesions to 85 per cent (29/33) (Table III). All T_1, T_2, T_3 lesions have not recurred and the one failure of a T_3 lesion listed was an extension, we believe, from failure to control nodal disease and reinvasion of tongue. More gratifying has been the ability to

TABLE I

APO: DISTRIBUTION BY SITE
PRIMARY SQUAMOUS CELL CANCERS

Nasopharynx	5
Oropharynx	14
Laryngopharynx	10
Oral cavity	16
Total	43

APO = Atmospheric oxygen.

TABLE II

APO: PRIMARY SQUAMOUS CELL CANCER OF HEAD AND NECK

April 1964-April 1967 (1-4 yr. follow-up)

Alive without disease	17	23	
Dead without disease*	5	5	67% Control
Alive with disease†	2	3	
Dead with disease	9	12	52% Survival
	33‡	43§	

* All autopsy proven. † 1° Controlled, metastatic.
‡ Eligible for 1 year survival.
§ All patients.

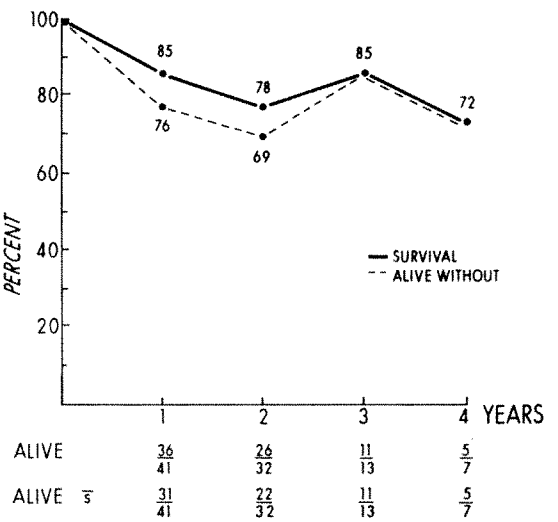


FIG. 3. Survival rates for head and neck cancer (University of Rochester series).

TABLE III

APO: PRIMARY SQUAMOUS CELL CANCER OF HEAD AND NECK

	Local Control		
T_1	2/2		4/4
T_2	5/5		9/9
T_3	10/11		12/14
T_4	12/15		12/16
	29/33*	85%	37/43†

* Eligible for 1 year survival.
† All patients.

cause regression and disappearance of rather extensive T_4 lesions (3 of 15 failed) in 80 per cent of our cases (Fig. 4, *A* and *B*; and 5, *A–D*). The ability to control nodal disease has been less successful, but this has not been a function of the degree of nodal involvement alone. The 63 per cent regression and control rate is a good result (Table IV). Although none of the N_0 lymph nodes are included in the percentage control figure, microscopic disease probably was present in a number of patients and no nodal disease has appeared subsequently. This may be of significance since there were large T_3 and T_4 lesions in which the neck was treated electively.

The reasons for failure are listed in Figure 6 and Table V but can be summarized as due to four reasons: failure to control the primary lesion, failure to control the lymph nodes, metastases and severe necrosis.

1. *Local Failures.* Three of the 4 patients had extensive infiltrative tongue cancers of the arterior two-thirds. Two of these developed necrosis, one at the conclusion of treatment and one 6 months after healing and completion of treatment. The one T_3 failure listed had healing of the local site of origin but recurrent neck disease after radical dissection resulted in re-invasion into base of tongue. There was one massive T_4 tonsillar, soft palate cancer that extended beyond the treatment field into the lacrimal duct presenting as an anterior mass below the lower eyelid.

Other points of importance are that all failures to control primary lesions were associated with a failure to control lymph nodes, and in two instances metastases to lung occurred.

Only 1 patient, a T_4 pharyngeal lesion

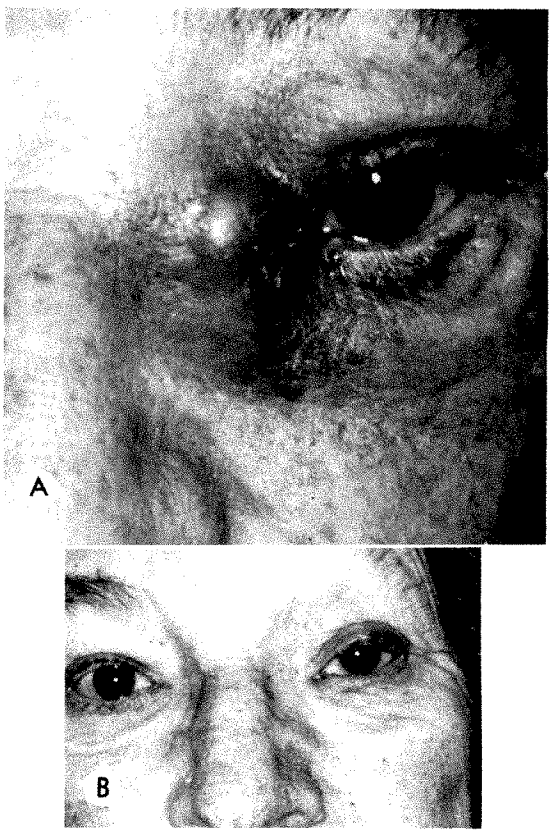


FIG. 4. *Advanced ethmoid carcinoma*—T_4, N_2. This 75 year old white female presented with proptosis of the left eye and limitation of ocular motion in every direction. (*A*) There is an obvious swelling at the left of the lateral aspect of the bridge of the nose extending to the medial canthus of the left eye. This was diagnosed as an epidermoid carcinoma of the ethmoid sinus with orbital invasion and cervical lymph node metastases, classified as a T_4, N_2 lesion. Roentgenograms revealed extensive involvement to the base of the skull and medial left orbital wall and the region of the ethmoid and frontal sinuses. This patient was treated with anterior and lateral fields delivering a total tumor dose of 7,025 rads (maximal) and a minimal dose of 5,450 rads in 51 days with 2 mev. roentgen radiation. Oxygen breathing was performed throughout the course of treatment. A separate anterior neck field was utilized delivering a dose of 5,400 r a depth of 3 cm. A dramatic regression of the enlarged lymph nodes and of the primary lesion occurred. (*B*) The patient has remained free of disease for 2 years.

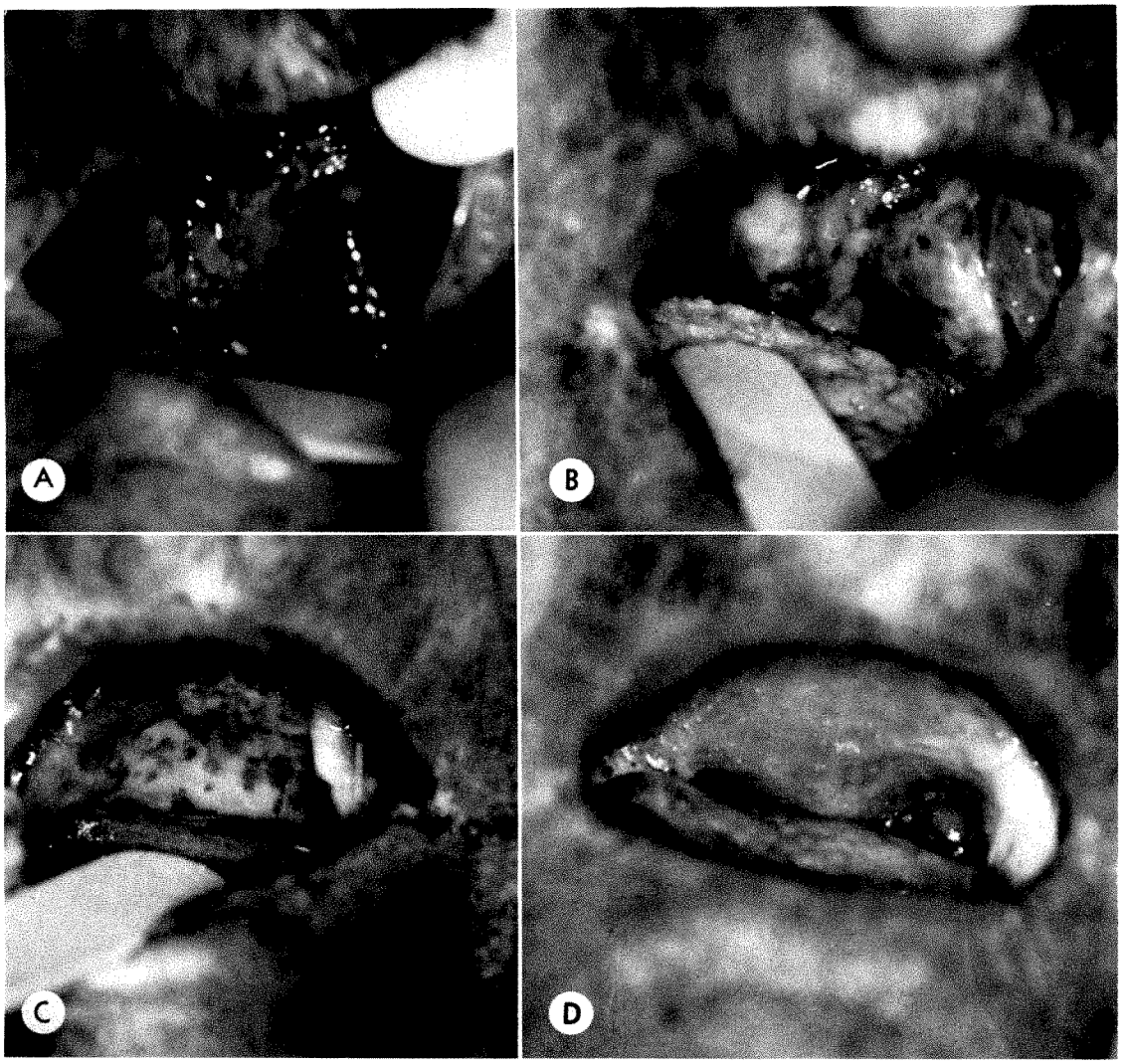


Fig. 5. *Advanced tonsillar fossa carcinoma*-T_4, N_0. (*A*) This 84 year old man presented with a massive lesion involving the region of the left tonsillar fossa extending into the soft palate and onto the buccal mucosa. Roentgenograms revealed invasion into the mandible. No lymph nodes were palpable in the neck. The pathology was that of a carcinoma of the palatine tonsil, classified as T_4, N_0. This patient was treated with opposed lateral fields measuring 7.5×11 cm. with 2 mev. roentgen radiation. (*B*) After delivering a tumor dose of 2,000 rads in 14 days, marked mucositis developed over the carcinoma as regression took place. No changes were noted in the normal tissues. At the 4,000 rad level, a brisk mucositis developed over the normal mucosa in the region of the palate and buccal area. There was a virtual total disappearance of the cancer. The reaction was so brisk that an interruption in therapy was required for 2 weeks. (*C*) Treatment was resumed on the 45th day and a total dose of 7,000 rads was delivered in 66 days. Complete healing has taken place during a month's time. (*D*) The patient is free of disease at the primary site and neck more than 2 years after the completion of treatment with the development of metastatic pulmonary lesions.

who did not complete a full course of therapy (4,000 r) was excluded in our results.

2. *Nodal Failures.* There were 6 instances of nodal disease recurring or persisting following irradiation. Three of these cases were N_3 with fixed lymph nodes and large primary lesions, 2 others were N_1 lymph nodes, one of which recurred after surgery, and one was an N_2 lymph node with a T_4 lesion. Three of these cases had associated pulmonary metastases. In the 2 cases in

TABLE IV

APO: PRIMARY SQUAMOUS CELL CANCER OF HEAD AND NECK

	Nodal Control		
N_0	17/17		23/24
N_1	3/5		4/7
N_2	1/2		1/2
N_3	6/9		7/10
	10/16*	63%	35/43†

* Eligible for 1 year survival.
† All patients.

which the primary lesion was controlled, neck dissection revealed positive lymph nodes and was controlled after the planned surgical procedure.

3. *Metastatic Failures.* There were 8 instances of distant metastases, most commonly recognized in lung prior to death but very widespread at postmortem examination. It is noteworthy that 5 of 8 of the metastatic cases had no primary or nodal cancer residuum.

4. *Necrosis.* The cases with tumor control and necrosis are worth further analysis, since the 7 cases constitute radiotherapeutic complications (Table v). There were 4 patients who were thought to have major recurrent or persistent disease but surprisingly all of them have healed (Fig. 7, *A* and *B*). One posterior pharyngeal ulcer required carotid ligation and the patient has survived $3\frac{1}{4}$ years, another case had base of tongue necrosis at the site of gold grains, and the third case was one of necrosis of pterygoid bone which sequestered and healed. The fourth case had necrosis and fistula formation which occurred after a surgical decision to electively resect the site of the primary lesion in the tonsil, and neck dissection was made.

There were 5 minor cases of necrosis, 2 in soft tissue and 3 with denudation of alveolar mucosa and exposed bone. The principles of care were similar to those outlined by MacComb and Fletcher[22] and the necrosis healed spontaneously with meticulous oral hygenic measures and the application of the following prescription:

Hydrocortisone acetate	1%
Neomycin sulfate	5%
Zinc peroxide	5%
CMC jelly	4·5%
c̄ Varidase q.s. ad	30 ml.

Sig: Apply c̄ gauge pledget T.I.D. and after meals.

5. *Surgical Intervention.* There were different occasions for surgical procedures, some elective, some planned in combination with radiotherapy and some for radiotherapeutic failures (Table vi). Two primary sites resected yielded no evidence of tumor. Six neck dissections were done, 4 of which yielded negative lymph nodes. Some patients with positive lymph nodes who could have been benefited did not because of distant metastases and recurrence of neck disease.

In summary, there was a failure to control the cancer in 33 per cent of the cases, but only a small part of the failure rate

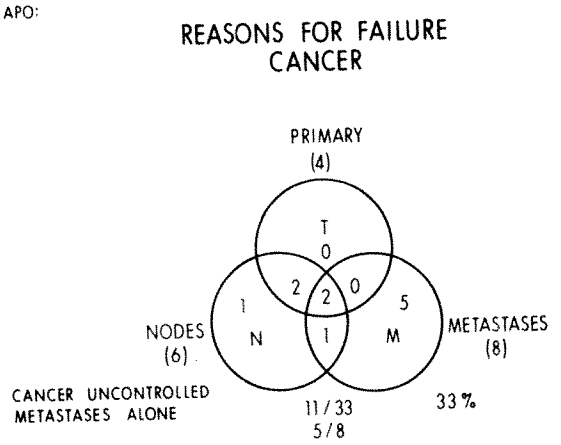


FIG. 6. *Venn diagram illustrating recurrent cancer and reasons for failure after radiation treatment.* The major reason for failure was metastasis and it is worthy of note that 5 of 8 or 33 per cent have metastases alone.

TABLE V

APO: REASONS FOR FAILURE NECROSIS

			Controlled	Alive
Major	4		3	3
Minor	5		5	5
Necrosis rate	9/33	27%		

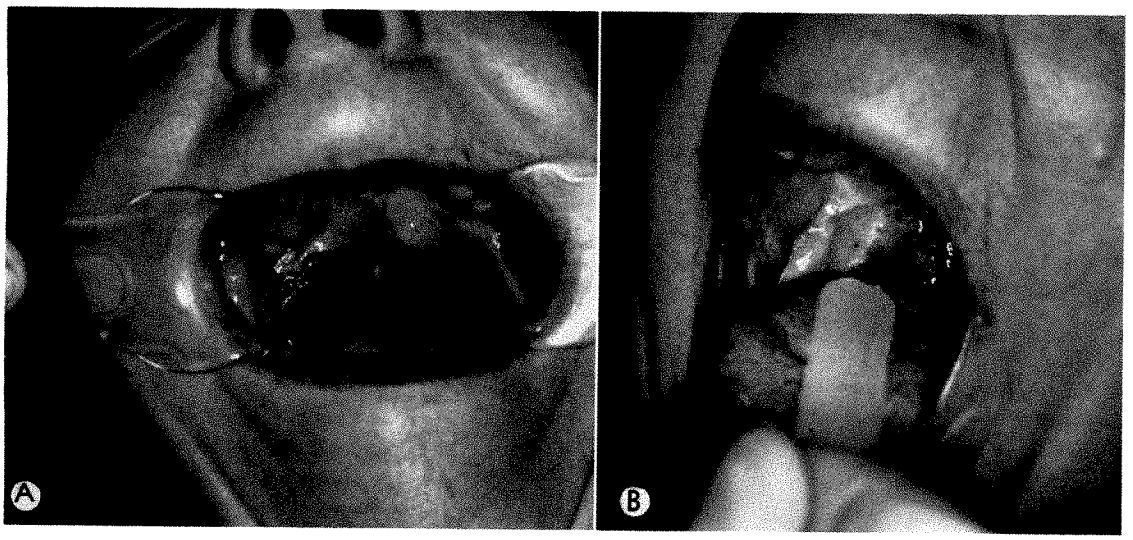


FIG. 7. *Advanced cancer of the right tonsillar fossa*-T_4, N_3. (*A*) This 60 year old female presented with a fungating lesion of the right tonsillar fossa which encroached upon the palate, right pharyngeal wall, base of tongue, right half of the uvula and the right posterior buccal mucosa. Two discrete nodes were present in the high and midportion of the right side of the neck. The largest node measured 2×2 cm. They were firm, painless and freely movable. The diagnosis was squamous cell carcinoma of the right tonsillar fossa, T_4, N_3. This patient was treated with 9×16 cm. fields to a total dose of 6,000 rads in 41 days. Oxygen breathing was conducted throughout therapy. Dramatic regression and total disappearance of the carcinoma occurred at approximately 3,000 rads. (*B*) A persistent ulcer in the tonsillar region remained at the end of therapy. This became very necrotic and heaped in appearance, suggesting recurrent carcinoma, within the next few months. The area sequestered and re-epithelized 1 year later. The patient is free of disease more than 4 years after treatment and has developed a second primary lesion, a cancer of the breast, treated recently with simple mastectomy.

represented an inability to control local or nodal disease. Complete (100 per cent) control occurred for:

(1) T_1, T_2, T_3, N_0
(2) T_4, N_0.

The failures were in T_3, T_4, N_1–N_3 cases, but half died of metastases without local or nodal disease. The potential value for hyperbaric oxygen was in those where the primary lesion and nodal disease were not controlled and those without metastatic disease. This occurred in 3/33 cases or 10 per cent of the group. The necrosis rate was

TABLE VI

APO: SURGICAL INTERVENTION

		1°	2°
Laryngectomy and neck dissection	1	−	+
Jaw–neck dissection	1	−	−
Radical neck dissection	4	0	3− 1+
Carotid ligation	1		
2 Primary lesions resected			
2 negative			
6 Neck dissections			
4 negative			
2 positive			
1 distant metastases			
1 recurrence in T and N			

27 per cent, but only 12 per cent were severe and all have subsequently healed or been controlled.

B. OTHER ATMOSPHERIC OXYGEN (APO) RESULTS IN THE LITERATURE

The best and most carefully controlled studies performed to date have been initiated by Kolstad and Bergsjo in Stage II cancer of the cervix.[19] A randomized study consisting of 208 cases of cervical cancer was divided between an air breathing control group and another group breathing oxygen at ambient pressure. Those patients breathing oxygen during external irradiation and radium insertion showed a distinct improvement in local control and a lesser degree of better survival (Fig. 8 and Table VII). The deaths due to local recurrence were 27.4 per cent for the control series *versus* 16.3 per cent in the oxygen breathers with external irradiation. The full advantage was offset to a degree by a larger number of deaths from distant metastases. The numbers are small, however, and are probably spurious. If oxygen breathing was limited to the radium application usually done first in this series, no advantage was detected. The gain in survival was 10 per cent (6.3/65.1 per cent) and in local control 15 per cent (11.1/72.6 per cent) which are calculated by dividing the difference by the control series.

The clinical trial of Synkavit and atmospheric breathing in lung cancer patients by Mitchell, Brinkley and Haybittle[28] failed to show any advantage to oxygen breathing with irradiation. The trial embraced a small number of patients and only measured mean survival. Our own impression is that there is an increase in mean survival, although it is not impressive. The reason, however, may be in the choice of tumor; that is, lung cancers metastasize readily and lead to early death despite local tumor control.

C. COMPARISON WITH HYPERBARIC OXYGEN (HPO) RESULTS IN LITERATURE

The differential effect of hyperbaric oxygen breathing on the therapeutic ratio is not precisely defined by the recorded experience to date. Some advantage to HPO may exist, but further investigation is

TABLE VII

CONTROLLED CLINICAL TRIAL WITH ATMOSPHERIC OXYGEN BREATHING DURING RADIOTHERAPY OF CARCINOMA OF THE CERVIX STAGE II
208 cases* followed 2 years

Treatment Group	Total No.	Dead with Local Recurrence		Dead from Distant Metastases		Alive with Local Recurrence		Alive without Signs of Active Disease	
		No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent
Control series air breathing	106	29	27.4	3	2.8	5	4.7	69	65.1
Oxygen breathing during radium irradiation only	49	16	32.7	1	2.1	2	4.1	30	61.1
Oxygen breathing during radium and external irradiation	49	8	16.3	4	8.2	2	4.1	35	71.4
Total	204	53	26.0	8	3.9	9	4.4	134	65.7

* Dead from intercurrent disease, not included in the Table: 4 cases. (Courtesy of P. Kolstad.)

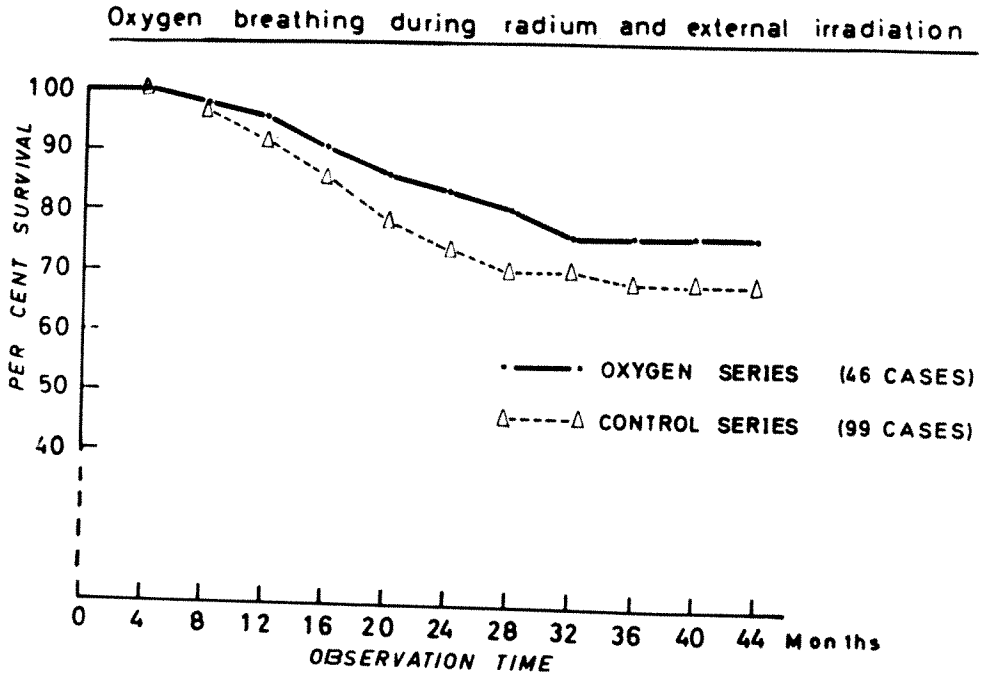


FIG. 8. Corrected survival rate in squamous cell carcinoma of the cervix Stage II. Patients dead from distant metastases and intercurrent disease are excluded. (Courtesy of P. Kolstad.)

required to establish this as a general clinical fact. At present, two approaches are being intensively investigated clinically:

1. A *short* intense fractionation scheme with high dose fractions (600 r in 6 sittings or 3,600 r in 18 days, two times weekly for 3 weeks) usually to large volumes—opposed fields 10×15 cm.

2. Regular *long* daily fractions with levels of 200 r daily tumor dose to total dose of 6,000 r in 6 weeks.

TABLE VIII

HPO *vs.* APO: RESULTS IN ADVANCED HEAD AND NECK CANCER

	van den Brenk[37] (6×500)	Rubin and Poulter
	Per Cent	Per Cent
Clearance of T_3, T_4	75	85
Clearance of N_2, N_3	78	64
Clearance of N_0, N_1, N_2, N_3	85	77
Radionecrosis	14	12
1 year cumulative survival	65	81

HPO = Hyperbaric oxygen.

Short Fractionation Schedule. The main exponents of this fractionation scheme are Churchill-Davidson[8] and van den Brenk.[37] A thorough analysis of a variety of schedules in 297 cases of advanced neoplastic disease (T_3, T_4, N_2 and N_3) of upper respiratory digestive passages using 4 mev. x rays with high pressure oxygen at 4 atmospheres by van den Brenk favors a schedule of 500 r × 6 in 0–17 days. More intensive daily fractions of 800 r or 1,000 r achieve comparable primary control rates but lead to high severe necrosis rates up to 51 per cent. The clearance of primary lesions ranges from 75 per cent to 87 per cent and of lymph nodes from 74 per cent to 81 per cent. The best result is shown in Table VIII for the 6×500 r scheme. The published results of Churchill-Davidson in a heterogeneous group of patients shows a 40 per cent 1 year survival decreasing to 9 per cent at 5 years. The results in both series are superior to the short fractionation scheme with air breathing.

The trial of Chang *et al.*[7] utilized two control groups with air breathing, one with

high daily dose fractions (1,000 r) and one with conventional doses (200 r daily). Local tumor control was comparable for HPO *vs.* air, *i.e.* 66 per cent *vs.* 75 per cent with a slight favoring for air breathing with high fractional doses, which was reduced to 25 per cent with conventional schemes. The glioblastoma multiforme trial of irradiation is difficult to evaluate and was not attempted.

The reports of Wildermuth,[39] Parker and Wootton,[24] and Plenk[25] are small in number, heterogeneous in cancer types and short in follow-up, suggesting that more trials should be continued on a controlled and randomized basis. It is fair to conclude, as Wildermuth has noted, "The results generally are less than spectacular." Complication rates are higher with short fractionation schemes.

Regular Fractionation Schedule. The two reports of HPO and regular daily fractionation at 200 r to total doses of 5,000–6,500 r are characterized by a higher metastatic rate. Johnson,[18] in a randomized study of advanced cervical cancer, has shown a higher local control for HPO *vs.* air, *i.e.*, 45 per cent *vs.* 20 per cent, but a higher mortality at 6 months, *i.e.*, 30 per cent *vs.* 15 per cent, respectively. In a pilot randomized study in bladder and lung cancer, Cade and McEwen[4] noted a poorer survival for patients breathing HPO during therapy due to an increase in metastases. The bladder cancer patients had a 40 per cent survival for HPO *vs.* 65 per cent survival with air, and lung patients were comparable in survival with a greater attrition rate for the HPO group.

In conclusion, the short fractionated scheme has not yielded a high cure rate for advanced lesions, although the control of primary and secondary lesions is achieved. No controlled study exists to indicate that short fractionation with HPO is better than current procedures, although it is better than short fractionated schemes in air. Results with air breathing utilizing long fractionation schemes in T_3 and T_4 head and neck cancers and cervical cancers range from 10 to 25 per cent[12,14,21] as compared to 14 per cent[8] at 5 years.

The second scheme has not yielded a higher survival rate owing to metastases which may occur at a higher frequency than in controls.[4,18]

A comparison of our results with the latest figures offered by van den Brenk,[37] as well as our present experience indicates that our therapeutic gain is comparable (Table VIII). The choice of cases will naturally affect the end results, and the placement of more T_4, and N_2, N_3 lymph node cases into a series is bound to lower survival results. Estimates of local and nodal control *versus* necrosis can establish radiotherapeutic advantages. The one advantage shown with hyperbaric oxygen breathing has been the control of nodal involvement. According to van den Brenk's recent studies[37] the rate of control of nodal metastases may be as high as 80 per cent.

V. FUTURE STUDIES

1. INTEGRATED SCHEME

The cornerstone of an effective radiation schedule is the initiation of tumor regression with the smallest possible daily dose (Fig. 9). Doses of 150 to 500 rads can be employed, depending upon the predicted response based on tumor histology, volume and location. It would be desirable to obtain measurements of tumor tissue oxygen tension clinically, but this is applicable only to a relatively few accessible tumors. There are three possible courses to consider, with oropharyngeal cancer as our reference cancer:

(a) If the tumor is radiosensitive and begins to regress during the first week of fractional radiotherapy, atmospheric oxygen breathing is worth adding to augment the improvement occurring in the microcirculation. This category includes the majority of patients.

(b) If the tumor is radioresponsive and only a slight response is seen in the first week, the patient should begin oxygen

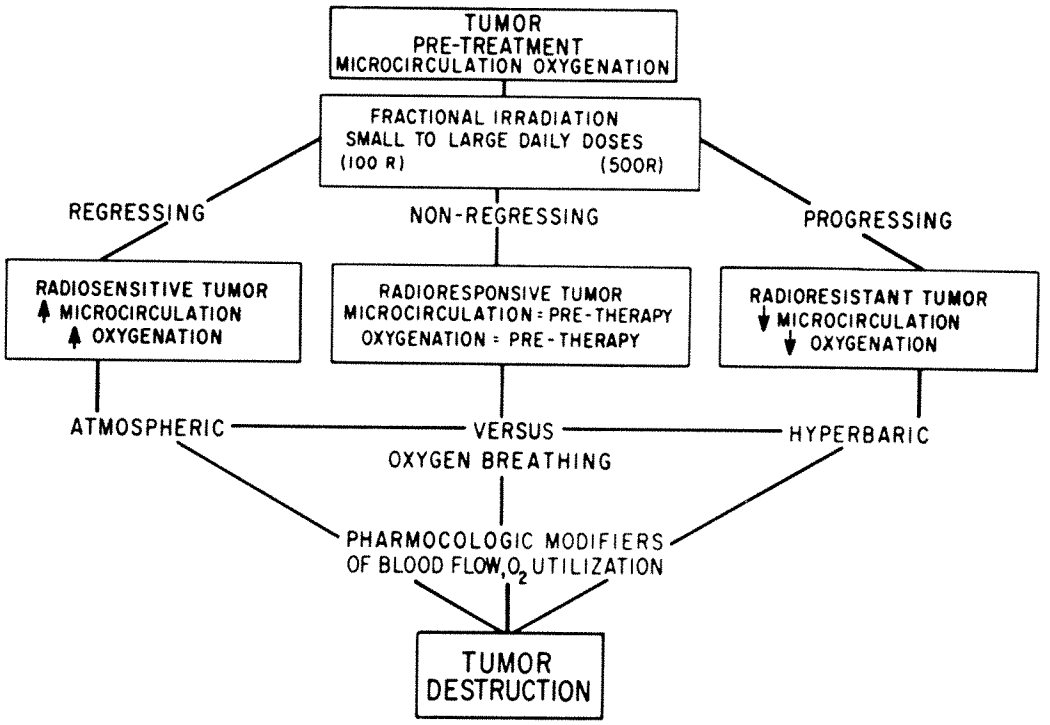


FIG. 9. Integrated scheme for atmospheric and hyperbaric oxygen breathing.

breathing at 1 atmosphere, but would benefit in the latter half of therapy with hyperbaric breathing, particularly if the tumor is slow in regressing.

(c) If the tumor is radioresistant, hyperbaric oxygen breathing could be used but may not be of much avail in obtaining regression. It is worth stressing that simply combining HPO and irradiation will not result in a dramatic reversal of inherent radioresistance. Chemotherapy may be of more value in this category of tumors, *i.e.*, methatrexate.

Combinations of atmospheric and hyperbaric oxygen breathing may be more efficient in tumor therapy than either approach alone. As tumor regression reaches completion clinically, the entire vasculature becomes defunctionalized and contributes to tumor destruction by cutting off its blood supply. At what point this state is reached has not been determined, since our experimental end point[29] was limited to tumors of 1 cm.^{3}, 10 per cent of the original tumor volume. A residuum of tumor 1.0 mm.^{3} in size may consist of 10^6 cells trapped in a fibrous hypoxic environment. Preliminary experimental work with animal tumors shows considerable variation in the vasculature in the end stages of tumor regression. This can, in our projection, be benefited by hyperbaric conditions. Confirmation of this concept is further supported in Suit and Maeda's experiments[32] relating tumor size to hyperbaric oxygenation. That is, the most efficient use of hyperbaric oxygenation does not occur as a rule in clinically palpable tumors 1.0 cm^3. in size but in smaller tumors of 1 mm.^{3}, or less.

The use of intense daily doses to small volumes for residuum of cancer at the end of a radiotherapeutic course with hyperbaric oxygen breathing is akin to supplemental radium or intense per oral cone techniques. The addition of 500 to 600 r in 2 sittings or 1,000 to 1,200 r in 1 sitting is both practical and feasible as a finessing or booster technique.

The main advantage of HPO breathing

may be in either priming or boosting the regular fractional therapy.

2. PHARMACOLOGIC MODIFIERS

Pharmacologic modifiers could also be employed to improve the circulation, as with the addition of 5 per cent CO_2. It is conceivable that exophytic portions of a tumor may regress and require only APO, and that HPO breathing would be required only in the last half of the treatment schedule in order to favorably alter the therapeutic ratio.

Pharmacologic modifiers could also be employed to improve tumor circulation by effecting blood flow. Utilizing polarographic methods of determining tumor oxygen tension, Cater *et al.*[5] have assessed tumor blood-flow changes and response to oxygen inhalation at 1 atmosphere. The most consistent finding was the increase in circulation and oxygenation as the blood pressure increased, except after the injection of norepinephrine, epinephrine and 5-hydroxytryptophamine (5-HT). When norepinephrine was given by slow perfusion, the blood pressure was elevated but tumor blood flow was reduced. Epinephrine raised the blood pressure but the effects on tumor blood flow were variable, as were the effects of the ganglion stimulating agents dimethyl-phenylpiperazine (DMPP) on hypertension. The vasodilators studied included acetyl choline, which increased tumor blood flow; nicotinic acid, which gave variable results; and isoprenaline and amylnitrite, both of which decreased blood flow. The effect of 5-HT to stop blood flow is striking, whereas the inflammatory agents bradykinin and kallikrein reduced tumor blood flow but increased the flow in the tumor capsule.

The inhalation of 5 or 10 per cent carbon dioxide with oxygen at atmospheric pressure increases tumor blood flow. Kruuv *et al.*,[20] in a series of careful studies on transplanted mammary cancers in C_3H mice, measured oxygen tension with platinum microelectrodes and blood flow indirectly (as reflected in surface temperature; thermal circulation index) by means of a Thermostromuhr bead thermistor. The inhalation of a mixture of CO_2 with oxygen at 1 atmosphere increased blood flow to necrotic tumor areas but not in well vascularized sites. Vasodilator drugs, such as chlorpromazine, isoproterenol and amylnitrite in air or 100 per cent oxygen, all decreased blood flow and oxygen tension of the tumor. A study designed to cure tumors with amylnitrite in oxygen was less successful than oxygen alone. The need to do careful physiologic studies is apparent before launching a clinical investigation program in which alternatives are followed randomly on speculative grounds.

The evidence presented in the studies of Du Sault[10] and co-workers[11] also favors the use of 5 per cent CO_2 and 95 per cent oxygen at atmospheric pressure. She[10] notes that pure oxygen breathing does not increase cures, whereas 5 per cent CO_2 added to atmospheric conditions yields a cure rate of 25 per cent, which is almost comparable to the gain of 37 per cent with 3 atmospheres of oxygen. The systemic changes with pure oxygen breathing were greater than with the mixture at atmospheric conditions, which differed from the observations reported by Kruuv *et al.*[20] If one were to choose between pure oxygen at 1 atmosphere and 5 per cent CO_2 with 95 per cent oxygen to do a clinical trial, the animal data would support the mixture. The value of vasodilator drugs and/or 5 per cent CO_2 needs elucidation in individual settings.

3. CONTROLLED AND COOPERATIVE CLINICAL TRIALS

The HPO therapy program has not yet translated the promising experimental results into superior clinical results utilizing short or conventional regular fractionation schemes. The expectation of spectacular or dramatic results is past. van den Brenk,[36,37] a meticulous and thorough investigator, has provided the most detailed results and has concluded, "HPO offers worthwhile improvement in the results of radiother-

apy—even if such results are to be in terms of palliation and relatively short term survival than long term cures." It is fair to say that no clinical HPO study to date shows a true gain in long term survival for advanced cancers in any anatomic site as compared to conventional fractionation techniques breathing air.

These statements are not intended to dimish the pioneer work of many workers in the field who must be admired for their courage and conviction in exploring the new frontiers of HPO breathing. The continued pursuit of further clinical trials with less radiobiologic and radiopathologic support than a decade ago needs careful consideration as to alternatives. We would echo the words of Buschke, that "it is probably worthwhile for a few institutions to investigate this procedure."[3]

DISCUSSION

The force of current evidence is that oxygen breathing at atmospheric pressures should be more fully explored because:

(1) A high degree of local control of primary lesions and lymph nodes can be obtained.

(2) The promise of clinical results suggests that a definite but small gain will occur (10–15 per cent) in survival.

(3) The radiobiologic and radiopathologic results support the finding of reoxygenation of tumors during conventional daily fractional irradiation.

(4) Studies can be mounted based on sound past experience as to reasonably "safe" dose levels and fractionation schemes.

(5) The cost and inconvenience are small to allow for almost universal application.

(6) Pharmacologic modifiers can be better utilized by taking advantage of physiologic changes during radiation treatment, such as 5 per cent CO_2.

(7) The use of HPO can be integrated into such a scheme to prime or finesse or boost the treatment. The last treatments may be the most critical in that the blood supply is ineffective and tumor hypoxia greatest at this stage.

(8) The untoward effects are minimal.

CONCLUSIONS

In conclusion, the changing perspectives with regard to oxygen breathing and radiation therapy have been explored in the light of current radiobiologic evidence and recent clinical results. This presentation should not be construed as opposing the use of HPO in practice. Rather, the use of oxygen breathing must be founded on a better understanding of the radiation pathologic and physiologic changes occurring in different tumors as treatment progresses. Anoxia is only one of the deterrents to successful control of cancer.[39] Those lesions which are not usually radiovulnerable according to Churchill-Davidson[8] will not respond better to HPO. Achieving local primary lesion and nodal control of advanced squamous cell cancers has not resulted in a parallel increase in survival due to metastases. The problem of an increase in metastases with oxygen breathing needs further study to elucidate the validity of this observation and the possible mechanisms.[9]

The promise of a gain in local control and survival exists by oxygen breathing (APO +5 per cent CO_2). We predict these gains will be substantial.

1. For localized (T_1, T_2) head and neck cancer and cervix cancer, local control can be achieved to the 90 per cent level ±5 per cent.

2. For advanced head and neck cancer (T_3, T_4) and cervix cancer (T_3, T_4) with lymph node involvement (N_1, N_2, N_3), the risk of metastases is higher but local and nodal control in a large number of patients can also be attained (50 per cent ±10 per cent).

3. The gain in survival, however, will be from 10–25 per cent over present base-lines.

It is because of these reasons that a national protocol is being developed by ourselves and Du Sault to randomize a variety of cancer patients utilizing ambient

oxygen breathing +5 per cent CO_2. Furthermore, the use of HPO for priming and boosting in such a program may be more logical than its current use with regular fractionation schemes, short or regular.

Philip Rubin, M.D.
Department of Radiation Therapy
Strong Memorial Hospital
260 Crittenden Boulevard
Rochester, New York 14620

REFERENCES

1. ANDREWS, J. R. Physical, biological and clinical aspects of fast neutron and other high LET radiations and implications for fast neutron beam clinical radiotherapy. In: Cellular Radiation Biology. Eighteenth Annual Symposium on Fundamental Cancer Research. Williams & Wilkins Company, Baltimore, 1965.
2. BERGSJO, P. Radiation-induced early changes in size and vascularity of cervical carcinoma: colpophotographic and clinical study. *Acta radiol.*, 1968, Suppl. 274.
3. BUSCHKE, F. Summary and closing remarks. In: Hyperbaric Oxygen and Radiation Therapy of Cancer. Edited by J. M. Vaeth. Proceedings of First Annual San Francisco Cancer Symposium. McCutchan Publishing Corporation, Berkeley, 1966, pp. 281–284.
4. CADE, I. S., and MCEWEN, J. B. Megavoltage radiotherapy in hyperbaric oxygen: controlled trial. *Cancer*, 1967, *20*, 817–821.
5. CATER, D. B., ADAIR, H. M., and GROVE, C. A. Effects of vasomotor drugs and "mediators" of inflammatory reaction upon oxygen tension of tumours and tumour blood-flow. *Brit. J. Cancer*, 1966, *20*, 504–516.
6. CATER, D. B., and SILVER, I. A. Quantitative measurements of oxygen tension in normal tissues and in tumours of patients before and after radiotherapy. *Acta radiol.*, 1960, *53*, 233–256.
7. CHANG, C. H., SEAMAN, W. B., and JACOX, H. W. Clinical aspects of hyperbaric oxygen and radiotherapy: New York experience. In: Hyperbaric Oxygen and Radiation Therapy of Cancer. Edited by J. M. Vaeth. Proceedings of First Annual San Francisco Cancer Symposium. McCutchan Publishing Corporation, Berkeley, 1965, p. 249.
8. CHURCHILL-DAVIDSON, I. Hyperbaric oxygen and radiotherapy: clinical experiences. In: Hyperbaric Oxygen and Radiation Therapy of Cancer. Edited by J. M. Vaeth. Proceedings of First Annual San Francisco Cancer Symposium. McCutchan Publishing Corporation, Berkeley, 1965, p. 207.
9. DETTMER, C. M., KRAMER, S., GOTTLIEB, S. F., APONTE, G. E., and DRISCOLL, D. H. Effect of increased oxygen tensions upon animal tumor growth. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1968, *102*, 804–810.
10. DU SAULT, L. A. Effect of oxygen in response of spontaneous tumours in mice to radiotherapy. *Brit. J. Radiol.*, 1963, *36*, 749–754.
11. DU SAULT, L. A., EYLER, W. R., and DOBBEN, G. D. Combination of oxygen and optimum fractionation in radiation therapy of adenocarcinoma. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1959, *82*, 688–692.
12. ENNUYER, A., and BATAINI, P. Résultats comparés de la radiothérapie à 200 kv. et de la radiocobalthérapie dans le traitement des tumeurs des voies aero-digestives supérieures. *Ann. Oto-laryng.*, 1966, *83*, 633–638.
13. EVANS, N. T. S., and NAYLOR, P. F. D. Effect of oxygen breathing and radiotherapy upon tissue oxygen tension of some human tumours. *Brit. J. Radiol.*, 1963, *36*, 418–425.
14. FLETCHER, G. H., MACCOMB, W. S., and BALLANTYNE, A. J. Radiation Therapy in the Management of Cancer of the Oral Cavity and Oropharynx. Charles C Thomas, Publisher, Springfield, Ill., 1962.
15. FOWLER, J. F. Biological Foundations of Radiotherapy. *International Congress. Excerpta Medica*, 1965, *105*, 731–737.
16. GRAY, L. H., CONGER, A. D., EBERT, M., HORNSEY, S., and SCOTT, O. C. A. Concentration of oxygen dissolved in tissues at time of irradiation as factor in radiotherapy. *Brit. J. Radiol.*, 1953, *26*, 638–648.
17. INCH, W. R., MCCREDIE, G. A., and KRUUV, J. Effect of breathing 5% carbon dioxide and 95% oxygen at atmospheric pressure on tumour radiocurability. *Acta radiol.* (Ther.), 1966, *4*, 17–25.
18. JOHNSON, R. J. R. Gynecological cancer treated with cobalt under hyperbaric conditions. In: Hyperbaric Oxygen and Radiation Therapy of Cancer. Edited by J. M. Vaeth. Proceedings of First Annual San Francisco Cancer Symposium. McCutchan Publishing Corporation, Berkeley, 1965, p. 185.
19. KOLSTAD, P., and BERGSJO, P. To be published.
20. KRUUV, J. A., INCH, W. R., and MCCREDIE, J. A. Blood flow and oxygenation of tumors in mice. I. Effects of breathing gases containing carbon dioxide at atmospheric pressure. *Cancer*, 1967, *20*, 51–59.
21. LEDERMAN, M. Cancer of pharynx: study based on radiation treatment. *J. Laryng. & Otol.*, 1967, *81*, 151–172.
22. MACCOMB, W. S., and FLETCHER, G. H. Cancer of the Head and Neck. Williams & Wilkins Company, Baltimore, 1967.

23. MITCHELL, J. S., BRINKLEY, D., and HAYBITTLE, J. L. Clinical trial of radiosensitizers, including Synkavit and oxygen inhaled at atmospheric pressure. *Acta radiol.* (Ther.), 1965, *3*, 329–341.

24. PARKER, R. G., and WOOTTON, P. Physiological evaluation of patients subjected to hyperbaric radiation therapy. In: Hyperbaric Oxygen and Radiation Therapy. Edited by J. M. Vaeth. Proceedings of First Annual San Francisco Cancer Symposium. McCutchan Publishing Corporation, Berkeley, 1965, p. 139.

25. PLENK, H. P. Hyperbaric radiation therapy: Salt Lake City experience. In: Hyperbaric Oxygen and Radiation Therapy of Cancer. Edited by J. M. Vaeth. Proceedings of First Annual San Francisco Cancer Symposium. McCutchan Publishing Corporation, Berkeley, 1965, p. 257.

26. REINHOLD, H. S. Post-irradiation behaviour of transplantable solid tumours in relation to regional oxygenation. *Deutsch. Gesundh.*, 1965, *20*, 216–220.

27. RUBIN, P. Microangiography: facts and artifacts. *Radiol. Clin. North America*, 1964, *2*, 499–513.

28. RUBIN, P. Atmospheric oxygen breathing and fractionation to enhance radiation effect. In: Conference on Radiobiology and Radiotherapy. National Cancer Institute Monograph 24, 1967.

29. RUBIN, P., and CASARETT, G. W. Microcirculation of tumors. I. Anatomy, functions, and necrosis. II. Supervascularized state of irradiated regressing tumors. *Clin. Radiol.*, 1966, *17*, 220–229, 346–355.

30. RUBIN, P., and CASARETT, G. W. Clinical Radiation Pathology. W. B. Saunders Company, Philadelphia, 1968.

31. SUIT, H., LINDBERG, R., SUCHATO, C., and OZENNE, A. Radiation dose fractionation and high pressure oxygen in radiotherapy of DBA mouse mammary carcinoma. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1967, *99*, 895–899.

32. SUIT, H., and MAEDA, M. Oxygen effect factor and tumor volume in C_3H mouse mammary carcinoma: preliminary report. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1966, *96*, 177–182.

33. THOMLINSON, R. H. Experimental method for comparing treatments of intact malignant tumours in animals and its application to use of oxygen in radiotherapy. *Brit. J. Cancer*, 1960, *14*, 555–576.

34. THOMLINSON, R. H. Personal communication, 1968.

35. THOMLINSON, R. H., and GRAY, L. H. Histological structure of some human lung cancers and possible implications for radiotherapy. *Brit. J. Cancer*, 1955, *9*, 539–549.

36. VAN DEN BRENK, H. A. S. Increased radiosensitivity of skin in humans irradiated in 4 ATA oxygen pressure. In: Hyperbaric Oxygen and Radiation Therapy of Cancer. Edited by J. M. Vaeth. Proceedings of First Annual San Francisco Cancer Symposium. McCutchan Publishing Corporation, Berkeley, 1965, p. 177.

37. VAN DEN BRENK, H. A. S. Hyperbaric oxygen in radiation therapy: investigation of dose-effect relationships in tumor response and tissue damage. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1968, *102*, 8–26.

38. VAN PUTTEN, L. M., and KALLMAN, R. F. Effect of pre-irradiation on ratio of oxygenated and anoxic cells in transplanted mouse tumor. In: Hyperbaric Oxygen and Radiation Therapy of Cancer. Edited by J. M. Vaeth. Proceedings of First Annual San Francisco Cancer Symposium. McCutchan Publishing Corporation, Berkeley, 1965, p. 29.

39. WILDERMUTH, O. Problems in management of patients with hyperbaric radiotherapy. In: Hyperbaric Oxygen and Radiation Therapy of Cancer. Edited by J. M. Vaeth. Proceedings of First Annual San Francisco Cancer Symposium. McCutchan Publishing Corporation, Berkeley, 1965, p. 161.

ISOTOPE RENOGRAPHY AND RENAL ARTERIOGRAPHY IN THE EVALUATION OF RENAL TRANSPLANTS*

By HAROLD D. DAVIDSON, M.D., MERLE K. LOKEN, PH.D., M.D., *and* KURT AMPLATZ, M.D.
MINNEAPOLIS, MINNESOTA

IN RECENT years there has been an increasing interest in organ transplantation both in this country and abroad. Greater effort in the area of renal transplantation has paralleled this interest with less than perfect—but nevertheless encouraging—results.

When analysis of the data for this study was begun in late 1966, 53 patients had received renal transplants at the University of Minnesota Hospitals. Only 22 of these are living; the remainder died of causes usually related to renal failure and infections.

The "rejection reaction" is the term applied to the adverse response of the organism to the transplanted organ. This response may be modified or even eliminated if detected with the use of immunosuppressive agents and/or local radiation therapy. Among the modes of evaluation have been renal arteriography and isotope renography; a comparison of these procedures has provided interesting information.

MATERIALS AND METHODS

In a retrospective comparison analysis, 9 patients were found on whom both renal arteriography and isotope renography had been performed. One patient had two simultaneous transplants, and 1 patient had two sequential transplants. Two kidneys thus studied had arteriograms on two different dates. Therefore, this study is based on correlation of data from 13 renal arteriographies with appropriately related isotope renographies of 11 transplanted kidneys in 9 patients. It should be noted that all arteriographies were performed on patients who were considered abnormal at the time of the procedure.

For isotope renography a dose of 20 μc of iodine 131 hippuran is administered intravenously as a bolus.[3] Hippuran is sodium ortho-iodohippurate, which is neither produced nor destroyed by the body,[4] and is excreted unchanged in the urine. As such, it is similar to para-aminohippuric acid, which is excreted by the renal tubules.

The two probes of the employed dual ratemeter system have 2 inch diameter sodium iodide crystals. With the patient in a supine position one probe is placed over the transplanted pelvic kidney, and the other probe is centered over the heart as a vascular control. Each crystal is spaced 8 inches from the skin by a collimator. The system is connected through ratemeters and spectrometers to a strip chart recorder with overlapping pens. The radioactivity is monitored to a total of 30 minutes at a recorder rate of 3 inches per minute during the first minute and 12 inches per hour thereafter.

In most cases renal arteriography was performed via percutaneous transfemoral approach,[2] but 1 patient had a selective renal arteriography, and in 2 patients the translumbar route was used. A catheter was introduced percutaneously into the femoral artery and advanced to a point just proximal to the origin of the iliac artery anastomosis. Thirty to 40 cc. of 75 per cent diatrizoate was injected in 1.5 to 2 seconds, and serial roentgenograms were obtained at an exposure rate

* From the Department of Radiology, University of Minnesota Hospitals, Minneapolis, Minnesota.
Supported in part by NIH grant for cardiovascular research, No. 1 T12 HE 5853-01.

TABLE I

EVALUATION OF RENAL TRANSPLANTS

	Renogram Grade	Blood Urea Nitrogen (mg. per cent)	Creatinine (mg. per cent)	Creatinine Clearance (liters/24 hr.)
Grade I: Arteriograms				
J. K.	IV	108	17.8	—
Grade II: Arteriograms				
D. G.	III	57	4.3	13
D. J.	III	32	4.3	8
E. K.	IIc	90	14.2	11
Grade III: Arteriograms				
D. J.	III	83	6.4	1
B. M.	IIb	44	1.8	37
S. S.	IIa	29	2.0	41
D. W.	IV	85	8.3	1
D. W.	IV	60	6.7	1
Grade IV: Arteriograms				
B. M.	IV	93	16.1	1
V. W.	IV	86	11.5	—

of 3 per second for 2 seconds and 1.5 per second for the following 3 seconds using a cut film changer. This provided a series of 10 roentgenograms demonstrating not only anatomic information of the renal arterial tree but also transit time of contrast medium and nephrographic effect.

The patients' blood urea nitrogen (BUN), serum creatinine, and creatinine clearance were the guidelines for comparison of clinical status with arteriographic and renographic observations.

RESULTS

The renal arteriograms were graded on the basis of flow-rate, peripheral vascular "pruning," and presence or absence of renal artery filling—essentially the criteria of Alfidi *et al.*[1] A beaded appearance of the renal artery occurred only in 1 patient, and vascular bowing, a presumed sign of edema, was identified in only 1 patient. If the renal artery filled, every patient exhibited a good nephrogram.

Grade I: Normal.
Grade II: Some pruning and minimal decrease in flow rate.
Grade III: Severe pruning with or without beading but with marked decrease in flow rate.
Grade IV: Non-filling of the renal artery.

The isotope renograms were graded on the basis of rate of rise (normal time to peak less than 8 minutes), the relative peak (normal peak/standard more than 0.9), and the rate of fall (normal 20 minute/peak 0.3–0.5).

Grade I: Normal.
Grade II: a. Normal rise with prolonged fall.
b. Normal rise with little or no fall.
c. Prolonged rise with prolonged fall.
Grade III: Continual slow rise with no fall.
Grade IV: No rise beyond local vasculature (nephrectomy pattern).

Table 1 summarizes the data from all but 1 patient in the series. Only 1 patient had a normal arteriogram (Grade 1). On that date the isotope renogram was Grade IV. The BUN was 108 mg. per cent, and the serum creatinine was 17.8 mg. per cent. A creatinine clearance value was not obtained.

Three patients had Grade II arterio-

TABLE II

SINGLE CASE* EVALUATION OF RENAL TRANSPLANT

Date	Arteriogram	Renogram	Blood Urea Nitrogen (mg. per cent)	Creatinine (mg. per cent)	Creatinine Clearance (liters/24 hr.)
November 16, 1964	—	Left Grade I Right Grade I	18	1.1	166
November 18, 1964	Left Grade II Right Grade II	— —	22	1.4	63
November 19, 1964	—	Left Grade I Right Grade IIb	23	1.2	117
December 11, 1964	—	Left Grade I Right Grade IIc	10	0.9	85
December 31, 1964	—	Left Grade IIa Right Grade IIa	26	0.9	55
August 9, 1965	—	Left Grade IV Right Grade III	80	3.5	13

grams. Two of them had Grade III renograms, and 1 had a Grade IIc tracing. In all 3 the values for the BUN and serum creatinine were elevated, and creatinine clearance was diminished severely (to less than 13 liters per 24 hours).

Among the 5 renal arteriograms classified as Grade III were found isotope renograms from Grade IIa to Grade IV, BUNs from 29–85 mg. per cent, serum creatinine values from 1.8–8.3 mg. per cent, and creatinine clearance values from less than 1 to 41 liters per 24 hours. The laboratory values paralleled the renogram analyses rather closely: (1) Grade IIa (BUN 29 mg. per cent, creatinine 2 mg. per cent, creatinine clearance 41 liters/24 hours); (2) Grade IIb (BUN 44 mg. per cent, creatinine 1.8 mg. per cent, creatinine clearance 37 liters/24 hours); (3) Grade III (BUN 83 mg. per cent, creatinine 6.4 mg. per cent, creatinine clearance less than 1 liter/24 hours); and (4) 2 Grade IV patients (BUN 60–85 mg. per cent, creatinine 6.7–8.3 mg. per cent, creatinine clearance less than 1 liter/24 hours).

There was occlusion of the renal arteries of 2 kidneys (arterial Grade IV). In both of these instances the renograms were also Grade IV (nephrectomy pattern). In each instance the BUN exceeded 85 mg. per cent; the serum creatinine was over 11.5 mg. per cent, and the creatinine clearance was less than 1 liter per 24 hours.

One patient (S. F.) had bilateral renal transplants from a single cadaver donor (Table II). Selected renograms on this patient are shown in Figure 1, *A-D*. The initial renogram was normal bilaterally (Grade I). At that time the laboratory studies also were normal. Two days later renal arteriograms were Grade II bilaterally; the creatinine clearance was decreased to 63 liters per 24 hours, but the BUN and creatinine were unchanged. The following day a repeat renogram was Grade I on the left and Grade IIb on the right. There was no change in laboratory values. Over the succeeding 5 weeks some recovery of function occurred on the right by isotope renography with some deterioration on the left to a bilateral Grade IIa. Laboratory values were 26 mg. per cent, 0.9 mg. per cent, and 55 liters/24 hours for BUN, creatinine, and creatinine clearance, respectively. No further arterio-

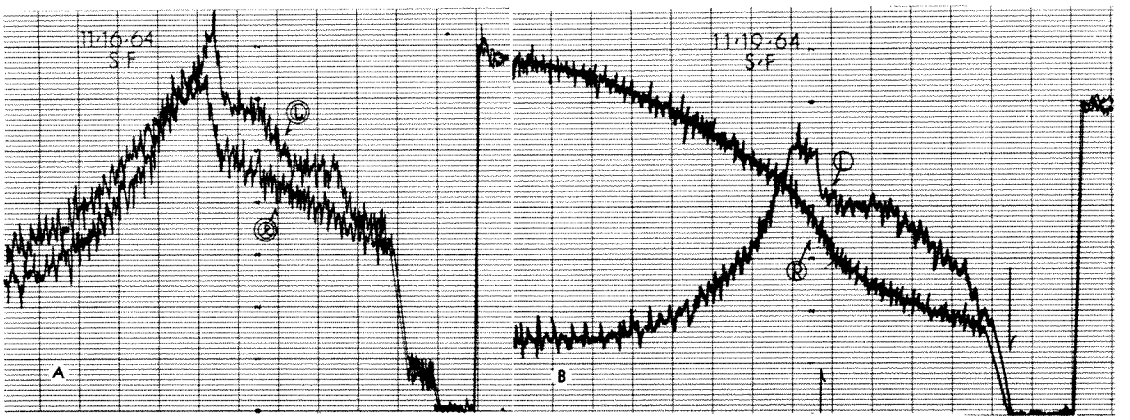


FIG. 1. Patient S. F. Selected renograms after bilateral kidney transplants. (*A*) The study on November 16, 1964 is essentially normal and was given Grade I rating bilaterally. The peak was obtained at 3.6 minutes for both kidneys. The ratio of 20 minute to peak for right and left kidneys, respectively, was 0.38 and 0.36. (*B*) The study performed 3 days later (November 19, 1964) shows that function of the left kidney remains normal whereas that on the right has deteriorated, suggesting a rejection reaction.

graphic studies were performed, but immediately prior to death the isotope renograms were Grades III on the right and IV on the left. Laboratory data were as follows: BUN 80 mg. per cent, creatinine 3.5 mg. per cent, and creatinine clearance 13 liters/24 hours.

DISCUSSION

The statistical validity of conclusions drawn from these data may be questioned. The volume of material is small, and there is the inherent relative lack of consistency characteristic of many retrospective studies. Nevertheless, certain conclusions seem indicated.

The case of J. K. (Fig. 2, *A* and *B*) illustrates that the renal arteriogram can be normal in the presence of severe renal failure in the post-transplant patient. The Grade IV renogram at that time correlates with the BUN of 108 mg. per cent and the serum creatinine of 17.8 mg. per cent (Table 1).

All patients with Grade II renal arteriograms, as illustrated by E. K. in Figure 3, *A* and *B* were in at least some degree of renal malfunction as indicated by BUNs

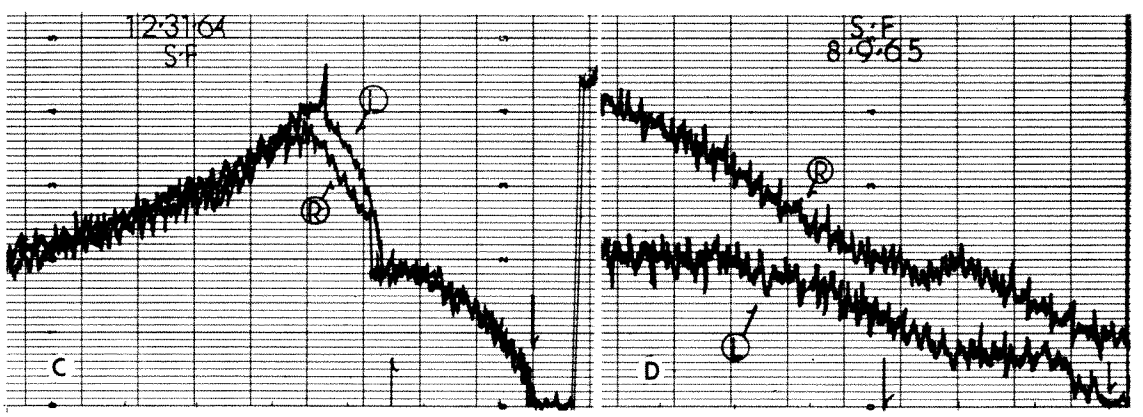


FIG. 1. (*C*) The renogram on December 31, 1964 shows some deterioration of function and was rated Grade IIa bilaterally. The peak times for right and left kidneys were nearly the same, averaging at 6.6 minutes. The ratio of 20 minute to peak values was 5.6 for the right and 0.63 for the left. (*D*) The final study on this patient was obtained on August 9, 1965 and shows marked depression of function bilaterally and was rated Grade III on the right and Grade IV on the left.

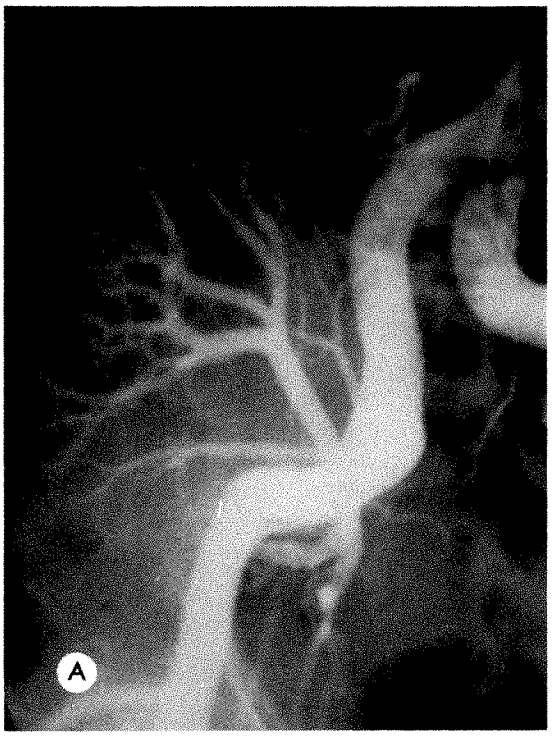


FIG. 2. Patient J. K. (*A*) Aortogram shows the transplanted kidney to be well perfused.

ranging to 90 mg. per cent and no creatinine clearance exceeding 13 liters/24 hours. The isotope renograms supported this premise with Grades III, III, and IIC.

Those with Grade III arteriograms in 2 instances, however, were experiencing better renal function than any of the patients whose arteriograms were Grade II. This is illustrated by patient S. S. in Figure 4, *A* and *B*. The findings on isotope renography again paralleled the laboratory data.

As would be anticipated, an occluded renal artery (Grade IV) produced a nephrectomy pattern (Grade IV) on the renogram.

In the case of S. F., the laboratory data give little information regarding individual renal function; however, it is shown that at about the time of the renal arteriogram, total renal function provided by the 2 transplanted kidneys was fairly adequate. Despite the symmetric appearance of the vasculature of the 2 kidneys on the Grade II arteriogram (Fig. 5, *A* and *B*), the isotope renogram showed a relative diminution of function on the right (Fig. 1*B*).

CONCLUSIONS AND SUMMARY

1. The renal arteriogram may be comparatively normal in the presence of severe renal failure in the patient with a transplanted kidney; therefore, it is of low reliability in the evaluation of these patients.

2. The patient status by isotope renography correlated well with patient status by laboratory analysis, proving that it is a

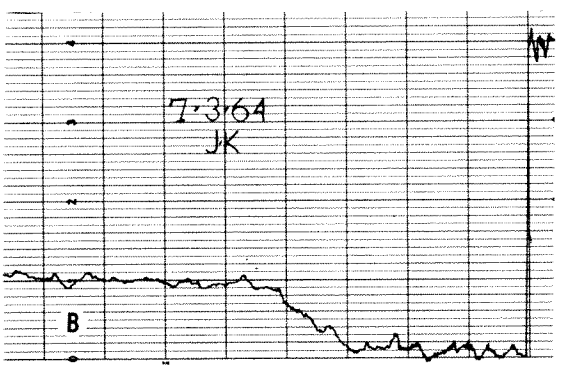


FIG. 2. (*B*) Renogram on the same date as the aortogram shows a nephrectomy pattern.

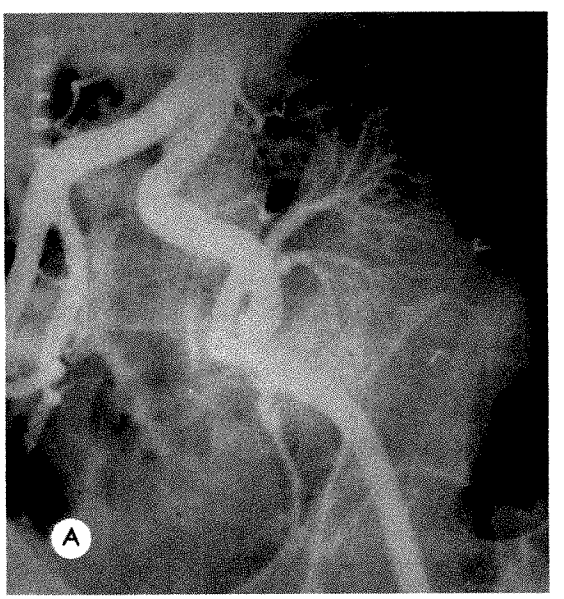


FIG. 3. Patient E. K. (*A*) Renal arteriogram shows a Grade II renal arterial pattern in a kidney transplanted into the left pelvis.

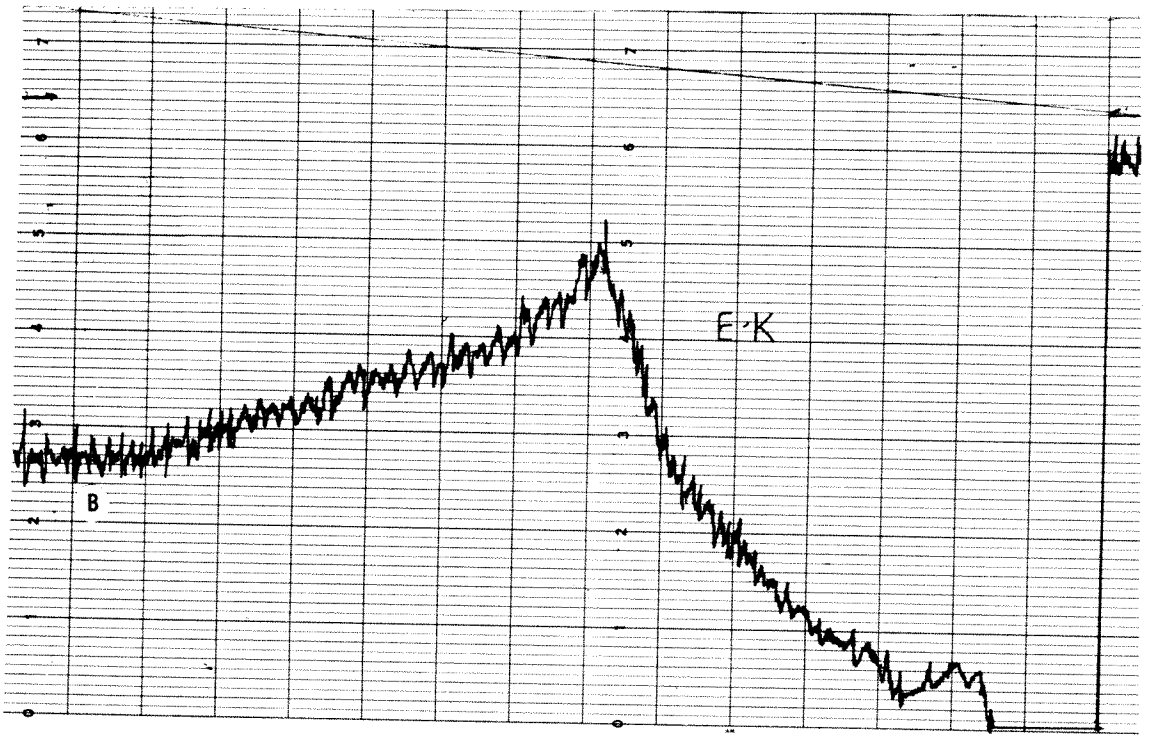


Fig. 3. (*B*) Renogram obtained on the same date was rated a Grade IIc.

test of high reliability in renal transplant evaluation.

3. The isotope renography is performed easily with minimum risk to the patient and is therefore a good survey device for renal transplant functional integrity.

4. As indicated above, a Grade IV isotope renogram may occur with either renal artery occlusion or severe extra-vascular renal parenchymal disease (Patients J. K., B. M., V. W.). The renal arteriogram will distinguish between these two possibilities, and this will direct patient management toward vascular occlusive disease or a rejection reaction.

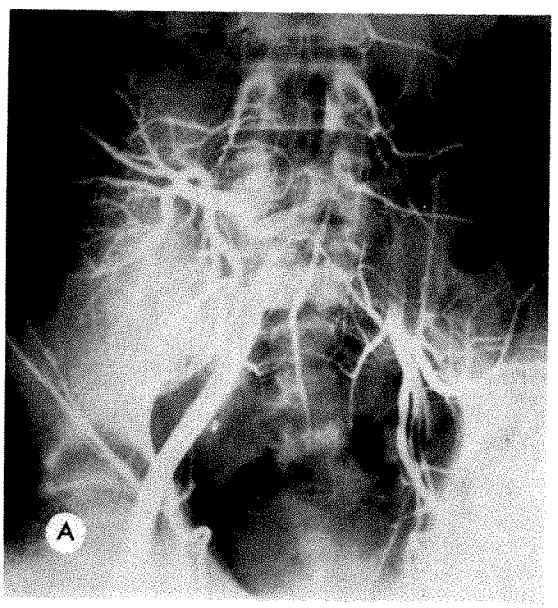


Fig. 4. Patient S. S. (*A*) Arteriogram shows a Grade III renal arterial pattern in patient who had a kidney transplanted into the right pelvis.

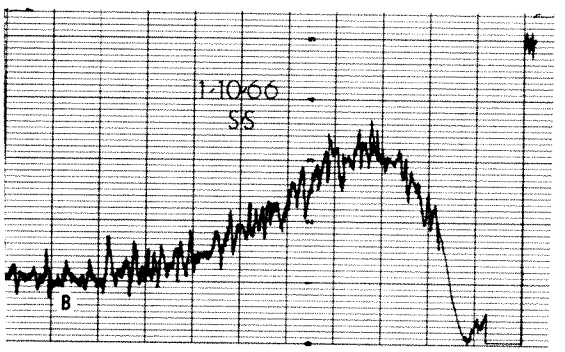


Fig. 4. (*B*) The renogram pattern on this patient was rated IIa.

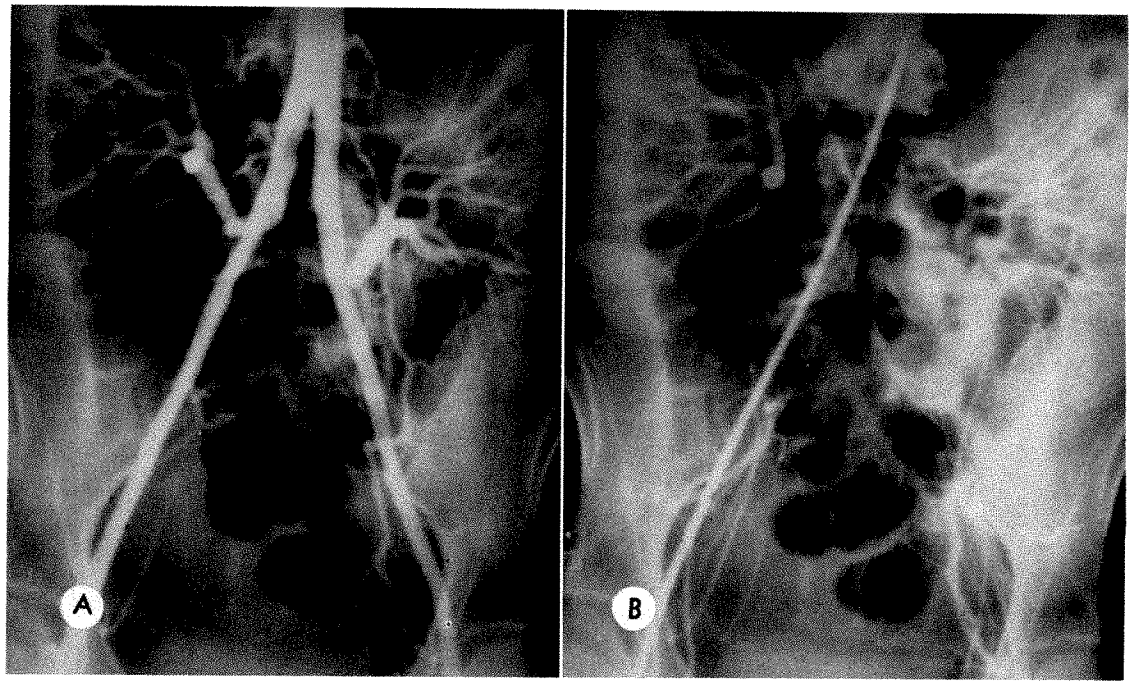


FIG. 5. Patient S. F. Two studies from an arteriogram in patient with bilateral renal transplant (see Figure 1). (*A*) The first was obtained during the arterial phase and (*B*) the second in the nephrogram phase. This was rated as a Grade II arterial pattern bilaterally at a time when the renal function on the right was deteriorating (Fig. 1*B*).

5. Isotope renography can be a routine procedure to follow patients with renal transplants. Its main information is physiologic. Renal arteriography, on the other hand, is a most important roentgenographic procedure for evaluating the anatomic status of the renal artery, and it appears to be indicated only in transplant failures.

Merle K. Loken, Ph.D., M.D.
Department of Radiology
University of Minnesota Hospitals
Minneapolis, Minnesota 55455

REFERENCES

1. ALFIDI, R. J., MEANEY, T. F., BUONOCORE, E., and NAKAMOTO, S. Evaluation of renal homotransplantation by selective angiography. *Radiology*, 1966, *87*, 1099–1104.
2. AMPLATZ, K. Personal communication.
3. LOKEN, M. K., STAAB, E. V., VERNIER, R. L., and KELLY, W. D. Radioisotope renogram in kidney transplants. *J. Nuclear Med.*, 1964, *5*, 807–810.
4. TAUXE, W. N., HUNT, J. C., and BURBANK, M. K. Radioisotope renogram (ortho-iodohippurate I^{131}): standardization of technique and expression of data. *Am. J. Clin. Path.*, 1967, *37*, 567–578.

VOL. 105, NO. 3

THE PLUGGING OF LEAKS IN RADIUM CONTAINERS*

By M. L. ROZENFELD, M.S.,† *and* E. W. MASON, B.S.‡
CHICAGO, ILLINOIS

THE extreme personnel health hazard due to possible radium contamination associated with the use of medical radium containers has long been recognized. Chief among the concerns was, and remains, the need to predict which containers are likely to leak radium. This prediction has generally been based on the leakage of radon, the gaseous daughter product of radium. It has been a widely held assumption that the absence of any radon leak indicates the absence of any holes. It has been further assumed that the existence of a radon leak indicates a hole that during normal usages would enlarge in time and finally allow radium to escape.

We have found both of these assumptions to be incorrect. First, holes in radium containers have frequently been found to be plugged with liquid, with the result that no detectable radon escaped. Second, the leak rate history of several containers shows that the holes do not enlarge over a period of several years. In addition, no detectable amount of radium leaked out of doubly encapsulated containers with holes so large that the radon leak rate approached the maximum possible.

Although a container that leaks radium would certainly also leak radon, our findings indicate that a radon leak generally is not a precursor of a radium leak. Therefore, radon leak testing alone will not significantly reduce the danger of a major radium spill. This can only be accomplished by a comprehensive program of radium management.

The finding that liquids will plug holes in radium containers makes the detection of such holes a more difficult task. Fortunately, since there is generally no associated radium leak, plugged holes in doubly encapsulated containers are not excessively dangerous. It is our opinion, therefore, that even though we have disproved the assumptions on which present radon leak testing procedures have been based, no major modification of these procedures is indicated.

PROCEDURE

The finding that liquids can plug radon leaks was made while performing the Hale test.[6] This test consists of submerging the radium container in a suspension of powdered activated charcoal in water. The container is left in a stoppered test tube holding the suspension for 24 hours. The radium container is then removed, the stopper replaced, and the activity retained in the test tube is assayed with a scintillation well counter. In order to determine the plugging efficiency of other liquids, modified Hale tests were performed with alcohol, ether, a solution of wetting agent, and kerosene.

The length of time that a hole remained plugged with a liquid was determined by repeatedly testing the radium container in test tubes with dry charcoal. This test was previously described by Frommhold and Schoknecht.[4] Except for the absence of any liquid, the procedure followed in this dry test is identical to that followed in the wet test described above.

A simple extension of this dry test allowed us to determine the approximate location of the holes in leaky radium containers. A 1 mm. thick rubber diaphragm was press-fitted into a length of glass tubing. A radium needle was then press-fitted part way into a small hole in the diaphragm. Charcoal chips were poured into each of the resulting compartments and both ends of the glass tube were sealed with rubber stoppers. After 24 hours, the charcoal from each compartment was poured

* From the Department of Radiology, The University of Chicago,† and the Argonne Cancer Research Hospital‡ (operated by The University of Chicago for the United States Atomic Energy Commission), Chicago, Illinois.

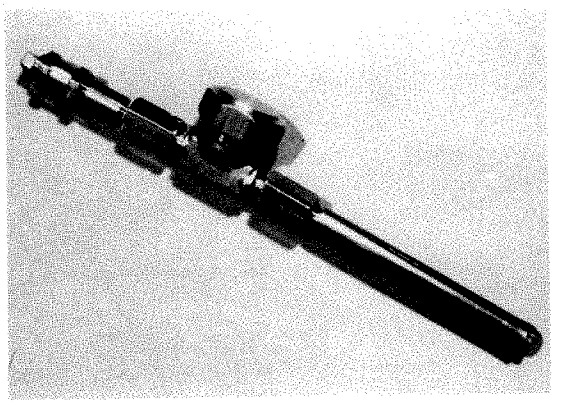


FIG. 1. Brass tube used to hold radium containers during heating.

out and counted separately. When the hole was entirely in one compartment, the ratio of activity between the two compartments might be as high as 5,000 to 1. When the hole was covered by the rubber diaphragm, the leak rate was greatly reduced and the activity in the two compartments was approximately equal.

The only procedure we found that would consistently open plugged holes involved heating the containers to 150° C. This heating must be performed with extreme caution because of the risk of rupture due to the increase in internal pressure at elevated temperatures.[3] In addition to retaining the radium in case of rupture, the procedure must be capable of concentrating small amounts of radon to detect leaks that are opened. These requirements are met by utilizing the brass tube shown in Figure 1 and adhering to the following procedure. One gram of preheated charcoal chips is placed in the bottom of the tube and held in place with glass wool. After the radium needle has been sealed in the tube, it is placed in an electric furnace which is housed in a dry box which, in turn, is located in a ventilating hood. A thermister regulator is used to maintain the temperature at 150° C. for 16 hours. The furnace supply voltage is, however, adjusted so that in the event of a failure of the regulator, the temperature does not exceed 160° C. After the furnace has been allowed to cool, the air in the dry box is pumped in a closed system through a membrane filter facing a germanium solid state alpha detector. If no alpha particles are detected, the dry box is opened, and the cover over the window of the brass tube is removed. A final visual inspection of the needle is made through the window before the plug in the brass tube is unscrewed and the needle removed. Any radon that escaped from an unplugged hole has by then been adsorbed on the cooled charcoal and can be assayed by inserting the brass tube in a scintillation well counter.

All of the above procedures involved the concentration of radon in tubes for assay in a well counter that contained a 1.5 inch high, 1.5 inch diameter NaI (Tl) crystal. The detector-photo tube combination, which was shielded by a minimum of 2 inches of lead, was connected to a high frequency nonoverloading pulse amplifier and scaler. The discriminator was operated in the integral mode and the discriminator setting and high voltage were adjusted for optimum signal to noise ratio.

This arrangement allowed us to measure the high activity from large leaks and still provided a minimum detectable true activity[1] of 23 pc at the 99 per cent confidence level for 1 minute source and background counts.

After a 24 hour leak test, the gamma activity can be measured at any time within the succeeding 3.5 hours with a maximum error of only 2 per cent due to nonequilibrium of the radon daughters.

For short sealing periods, however, sufficient time must be allowed between the removal of the radium and the counting of the test tube to allow for the build-up of the gamma emitting daughters. Since the radium containers are frequently sealed in the test tubes for other than 24 hour periods, all the results were converted into the equivalent daily leak rate. Calibration of the counter with a sealed National Bureau of Standards radium solution allows the results to be expressed in microcuries per day.

In order to measure leak rates that fell

below the 23 pc detection level of the well counter, we used the alpha detector developed by Lucas.[8] This detector consists of a stainless steel chamber coated on the inside with ZnS, except for the quartz window used for coupling light pulses to a photomultiplier. Even though the chamber became contaminated, our system has a minimum detectable true activity of 0.05 pc at the 99 per cent confidence level for 1 hour source and background counts.

The radon leaking out of the radium container over a period of time must be concentrated and then transferred into the alpha detector. This is accomplished through the use of the transfer tube shown in Figure 2. The radium container is passed through the open stopcock into the quartz tube which contains a small quantity of charcoal. After 24 hours the radium container is removed and the transfer tube is assayed in a scintillation well counter. If activity is detected, the radon is discarded in order to prevent contamination of the alpha counter with radium D, E, and F. The leak rate can be obtained from the gamma count and the well counter calibration, for the dry tests described above. If no activity is detected, the transfer tube is connected to the previously evacuated low level counter and the valves are opened. In order to drive the adsorbed radon off the charcoal and into the counter, the quartz end of the transfer tube is heated for 3 minutes with a gas-air torch until the charcoal glows bright red. In order to further reduce the possibility of contamination, the measurement is terminated as soon as several thousand counts have been accumulated. The chamber is immediately evacuated with a mechanical vacuum pump and flushed several times with aged dry nitrogen. The system is calibrated through the use of a radium needle with a small consistent radon leak as measured with the dry test described above.

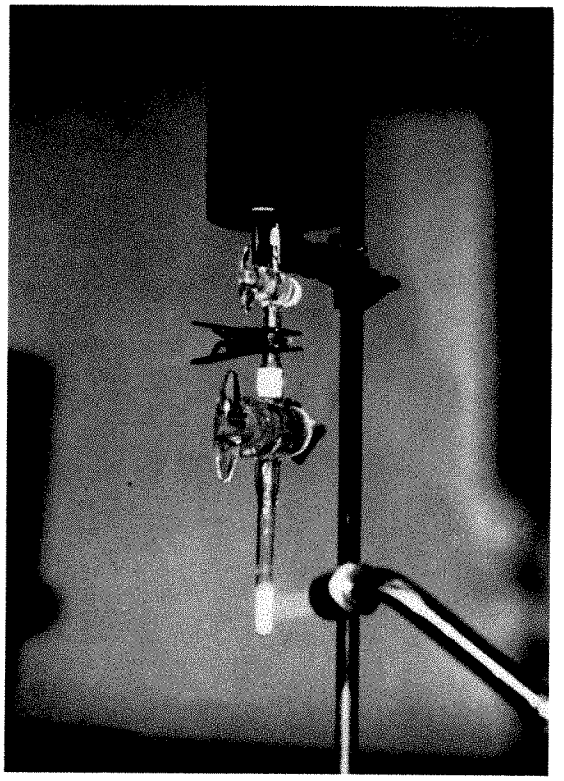


FIG. 2. Transfer tube, used for concentrating radon leaking out of a needle, is being heated to drive the radon into the Lucas counter.

OBSERVATIONS

A set of 15 doubly encapsulated medical radium containers with various leak rates has been subjected to a variety of leak testing procedures over a period of more than 2 years. These containers are doubly encapsulated in platinum-iridium alloy with compartmentalized inner cells and hard soldered end plugs.

The most important observation is that liquids can plug radon leaks in radium containers. Eight of the containers with the largest leak rates were immersed a total of 97 times in water, alcohol, ether, a solution of wetting agent, and kerosene. These immersions were accomplished by performing the Hale test or a modification of it using other liquids with and without charcoal. Twenty per cent of the immersions of containers that were leaking radon resulted in "permanent" plugging. That is, the needles remained plugged for at least 1 day after removal from the liquid. Fifty per cent of the immersions resulted in temporary plugging since the needles stopped leaking while in

the liquid but resumed leaking within 1 day after removal. In the remaining 30 per cent, the needles continued to leak radon into the liquid.

Some of these containers were re-immersed in liquid after they had become "permanently" plugged by previous immersions. Eighty per cent of these re-immersions had no effect, that is, the containers remained plugged. Only once did the container leak into the liquid, but became plugged again on removal. However, in 16 per cent of the re-immersions, the plugged containers were unplugged and leaked at their previous rate after removal from the liquid.

There is very little difference between the plugging and unplugging properties of the different liquids, so the results for all of them were combined. The only significant difference is the duration of the plug if it is left to dry. Two needles have remained plugged with water for more than 2 years. These needles have remained undisturbed except for periodic testing with dry charcoal. Two alcohol plugs, which were left to open of their own accord, lasted 2 weeks and 3 months, respectively. The 1 plug produced by ether dried out in 4 days. Apparently, the more volatile liquids dry out more rapidly, and thus produce less "permanent" plugs. The more volatile liquids, however, do not act as scavengers to remove water. Both water and alcohol opened water plugs only once in every 6 re-immersions. There was also no significant difference due to the lowered surface tension of the solution of wetting agent.

The only way of determining that a plugged hole existed was to open it. Leak rate alone could not distinguish between a small hole and a large hole that was plugged. One needle, which had a large hole with a maximum leak rate of 1.16 μc per day, released so little radon after plugging with water that it could not be detected by our well counter. In order to measure the small leak rate of this plugged needle, we used the alpha counting technique described above. The leak rate was 0.73 pc per day, which represents a reduction of more than 1.5 million.

In addition, the only method we found that would consistently open plugged holes required heating the containers to 150° C. overnight. One needle, which had survived 15 wet tests and 32 dry tests while maintaining a leak rate that averaged 1×10^{-3} μc per day over a period of 6 months, was found to have been plugged only after the heating process produced a consistent leak rate of 0.7 μc per day. Our experience with two other containers indicates that 150° C. does not create or enlarge leaks. These containers leaked radon at about 10^{-4} and 10^{-5} μc per day, respectively, before and after their heating period.

Figure 3 shows the leak rate history of one container to illustrate some of the effects described. The double dry test apparently plugged the hole in this container with a piece of rubber, which led to an oscillating leak rate. This figure also indicates that the maximum leak rate has not increased. All the containers showed this same feature. In no case was there an increase in the maximum leak rate over a 2 year period.

In order to determine the maximum possible leak rate, a small quantity of radium-barium sulfate was obtained from a manufacturer of medical radium containers. To ensure that the crystal structure of the sample was the same as in medical containers, the order specified that the salt be taken from a batch just before it was to be loaded into cells. The salt was deposited in the bottom of a small test tube and held in place with cotton wool. The quantity of radium that was delivered was determined to be 64 μg. and it liberated radon at a rate of 0.29 μc per day. That is, most of the radon remained trapped in the crystals and only 2.7 per cent of the radon generated each day was liberated.

Hahn[6] investigated the emanating power of various crystals and found that it depended on the salt, the crystal size, the lat-

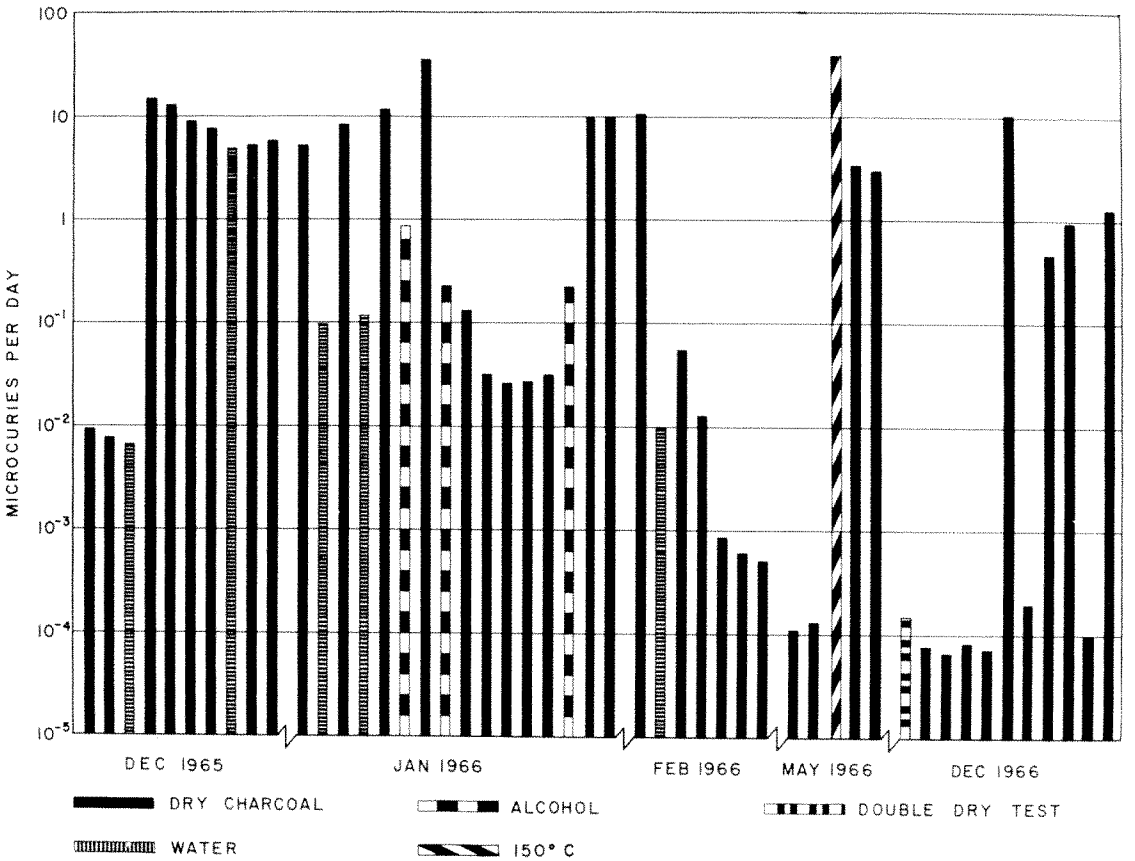


Fig. 3. Histogram of daily leak rate *versus* time of a typical doubly encapsulated radium container with a large hole under various test conditions.

tice structure, and the temperature. Our value of 2.7 per cent at room temperature indicates a very small crystal size.

The quantity of radon corresponding to this emanating power must be considered as the maximum possible leak rate at room temperature. For the 8 containers described above, the maximum measured leak rate, as a percentage of the maximum possible, varied from 8 to 49 per cent.

Radium wipe tests were then performed on the containers to determine if these large radon leaks were accompanied by radium leaks. Each container was wiped vigorously on a thick filter that was wetted by detergent solution. Gross alpha counting indicated measurable activity on most of the filters. Alpha spectrometry, however, showed that this activity was not from radium 226 but from polonium 210. This is the alpha emitting isotope in the group of radon daughters, radium D, E, and F.

Figure 4 is a composite alpha spectrogram; the lower trace was produced by the most active wipe and the upper trace was produced by a small radium source. The gain and base line were adjusted so that the energy in mev. could be read directly from the horizontal scale. The vertical scale is logarithmic with each division representing a factor of ten. This spectrogram should be considered in relation to the list of alpha emitting isotopes in the radium decay series shown in Table 1.

The beta emitters have been omitted and thorium C′ was included, although not a member of this series, since the radium was contaminated with mesothorium. The tho-

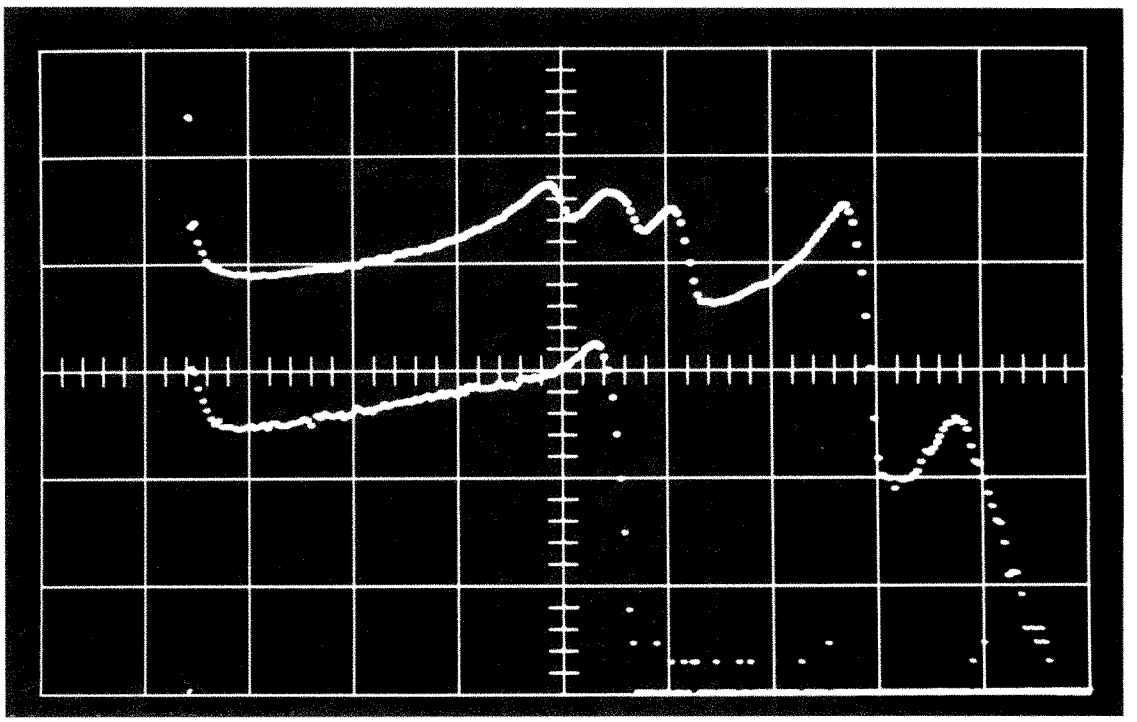


FIG. 4. Composite alpha spectrogram of a radium source (top) and a wipe test of a radium container with a large radon leak (bottom). The horizontal scale represents 1 mev. per division and the vertical scale is logarithmic with the bottom line representing 1 count.

rium C′ peak is the only one of the thorium series that appears, since the others are buried under the radium spectrum. The 5 alpha lines from radium, demonstrated in Table 1, appear as four peaks since those from radon and radium F are not resolved. The low energy tail on each peak is due to self-absorption and backscattering. The lower trace, which is from the wipe test, clearly shows 1 single peak, which is due to radium F. The activity on this wipe was determined to be 84 pc by calibration with a plutonium source. None of the wipes show any detectable activity due to radium.The minimum detectable activity of this system is 0.47 pc at the 99 per cent confidence level with an 800 minute sample and background counts.

The position of the hole in 3 of the largest leakers was determined by use of the double dry test described above. The hole was found to be within 4 mm. of the eye end of one needle, and within the same distance of the point of the other two. The correlation of these data with roentgenograms of these needles shown in Figure 5 indicates that the holes are probably due to faulty solder joints rather than cracks or faults in the tubes. The only fault visible in the roentgenograms is an open inner cell in one of the needles.

DISCUSSION

We have investigated the plugging properties of different liquids on a small sample

TABLE I

ALPHA PARTICLE EMITTERS IN RADIUM DECAY SERIES

Name	Symbol	Alpha Energy, mev.[12]
Radium	$_{88}Ra^{226}$	4.777
Radon	$_{86}Rn^{222}$	5.486
Radium A	$_{84}Po^{218}$	5.998
Radium C′	$_{84}Po^{214}$	7.680
Radium F	$_{84}Po^{210}$	5.298
Thorium C′	$_{84}Po^{212}$	8.780

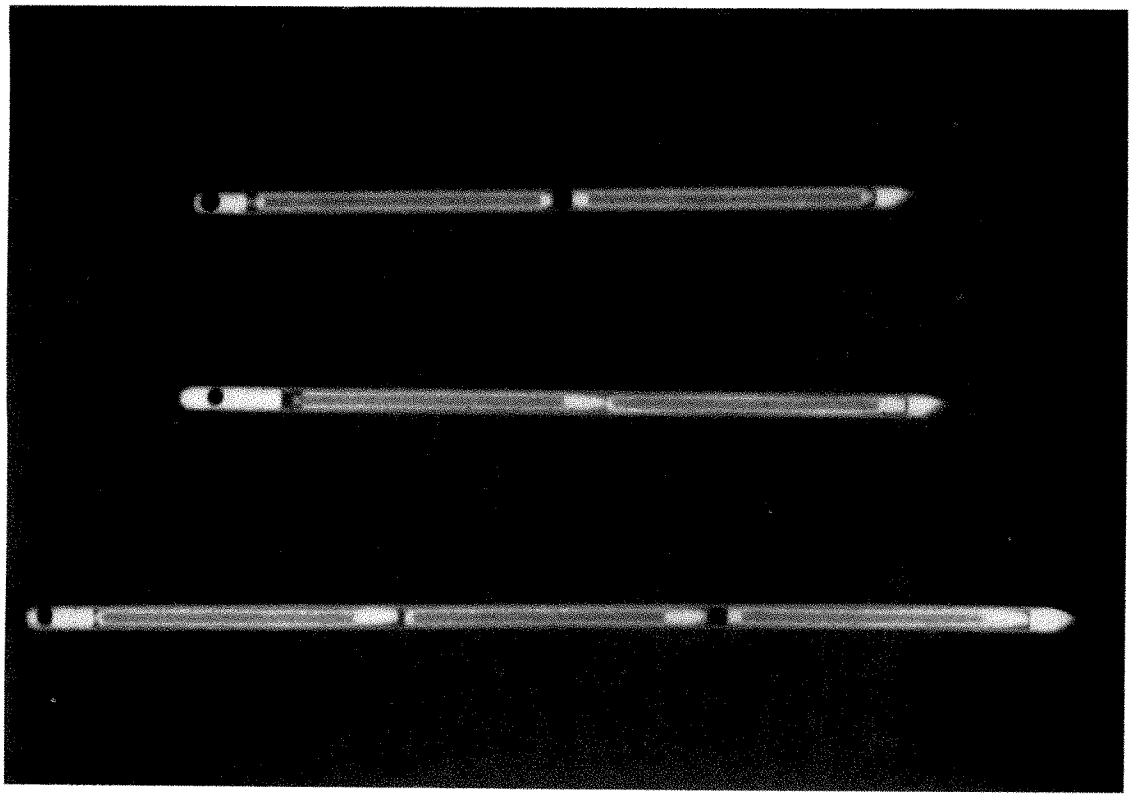


Fig. 5. Roentgenograms of radium needles showing details of construction and 1 major fault.

of only 8 needles with holes. All 8 of these needles, however, were plugged with a liquid at least once. This result places the 95 per cent confidence limit of the fraction of all needles with holes that can be plugged with liquids at 0.61. In other words, if these 8 needles can be considered a random sample from the entire population of needles with holes, then we can state with reasonable confidence that 61 per cent or more of that population can be plugged with liquids.

As of this writing, 9 out of a total stock of 173 doubly encapsulated containers, or 5.8 per cent, have been found to have a significant leak rate. That is, they have holes in both an inner cell and in the outer sheath. If we assume that the soldering process is similar for each and that the probability of a faulty solder joint is the same for each, then that probability is equal to the square root of .058 or about 24 per cent. This value must be considered as a minimum since, previous to this investigation, an unrecorded number of other containers in the stock were returned to the manufacturer because of radon leaks, and some containers with holes that are plugged with liquid might remain in the stock as yet undetected.

CONCLUSION

It has long been assumed that a hole in a radium container is formed and enlarges as the solder joint deteriorates. Lind[7] states, "The fact that those bonds remain tight for a time and then begin to leak suggests an aging effect, possibly due to radiation damage to the metal bond." Our observations on liquids plugging holes, combined with the long history of consistent maximum leak rates suggest another explanation. Holes, which are left in the solder joints during the manufacturing process, are then plugged by washing or plating solutions. Immediate radon leak testing will fail to

detect them. Over the years, however, the holes are unplugged by drying, or, more likely, by re-immersions in washing or sterilizing solutions. Thus, new leakers continue to be uncovered from a stock that has been regularly leak tested.

Holes in plugged radium containers presently in stock could be uncovered by heating them as described above. The dangers involved, however, lead us to advise that the heating procedure be done by the manufacturer or a central testing laboratory. The simplest, although most protracted, procedure of uncovering plugged holes, is to follow the present regulations of regular leak testing. Of the many radon leak tests available,[14] those that require immersion of the container in a liquid should be avoided.

The only observations relating to the much more serious problem of radium contamination gave negative results. None of our doubly encapsulated containers leaked radium even though their radon leak rates approached the maximum possible. In addition, the holes apparently were not enlarging. Concerning containers without holes, Van Roosenbeek and associates[13] have found that they are strong enough to withstand the pressure from helium build-up for more than 135 years.

There still remains, however, the problem of pressure due to the dissociation of water that might be sealed in the containers. Morgan[10] has calculated a maximum pressure build-up due to helium of 1.09 atmospheres per year. Thus the burst strength of the containers is about 147 atmospheres. Morgan also calculated that the 2 molecules of water of hydration per molecule at $RaBr_2$ would produce a pressure of 1,640 atmospheres after complete dissociation. This pressure is an order of magnitude greater than the burst strength and indicates the importance of adequate dehydration.

Most modern radium containers are filled with radium sulphate, an insoluble salt that does not retain water of hydration. Balarew and Kandilarow,[2] however, have shown that as much as one molecule of water per two molecules of $BaSO_4$ can be held mechanically within the capillaries of small crystals. Peltier and Duval[11] have shown that this water is not completely released until a temperature of 900° C. is attained. If radium sulphate has the same properties, then the maximum pressure due to the dissociation of water retained by incomplete dehydration of this salt is 410 atmospheres. This pressure also exceeds the burst strength. Morgan, however, quotes a manufacturer of medical radium containers as stating that as of the early 1960s the problem of inadequate dehydration has apparently been solved by the entire industry. Thus, doubly encapsulated radium containers of recent manufacture should be quite safe. Additional corroboration of this conclusion is obtained from a study of reported radium accidents:[9] old sources of single encapsulation in glass, or platinum with press-fitted end plugs were usually involved.

It is obvious, however, that any type of container would rupture if sufficiently abused. In the case of a rupture, the spread of radium might be reduced and decontamination simplified if it were sintered in ceramic. The same advantages might be obtained by utilizing large crystals of $RaSO_4$. In addition, two further advantages would arise.

Balarew and Kandilarow[2] have shown that large crystals of $BaSO_4$ retain only 2 per cent of the water retained by smaller crystals, while Hahn[5] pointed out that the emanating power of larger crystals is lower than that of small crystals.

These predictions have not been tested, since no medical radium containers have been filled with radium in ceramic or large crystal form, and of course no major spills have occurred with radium in these forms.

Even under these restrictions it is still possible to present several recommendations that could reduce the number and severity of future radium accidents.

All medical radium tubes and needles other than those doubly encapsulated in platinum-iridium with hard soldered end caps containing the sulphate salt should be

exchanged for modern containers of this type or one of the radium substitutes.

If new radium containers are purchased, the order should specify that the containers be heated to 150° C. overnight before the final leak test. Finally, all radium should be handled with the care and respect it deserves.

M. L. Rozenfeld, M.S.
Argonne Cancer Research Hospital
950 East 59th Street
Chicago, Illinois 60637

REFERENCES

1. Altschuler, B., and Pasternack, B. Statistical measures of lower limit of detection of radioactivity counter. *Health Physics*, 1963, *9*, 293–298.
2. Balarew, D., and Kandilarow, G. Ueber neuartige Mischkristalle. *Z. Anorg. Allgem. Chem.*, 1927, *162*, 344–348.
3. Cross, F. H., and Hunnings, G. Unusual radium incident in Nottingham. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1954, *72*, 989–994.
4. Frommhold, W., and Schoknecht, G. Messungen über die Dichtigkeit geschlossener radioaktiver Präparate. *Strahlentherapie*, 1959, *108*, 145–153.
5. Hahn, O. Applied Radiochemistry. Cornell University Press, Ithaca, N. Y., 1936, pp. 222–229.
6. Hale, J. Method for testing radium containers for leakage using well-type scintillation counter. *Radiology*, 1959, *72*, 105.
7. Lind, S. C. Care of radium salts. *Nucleonics*, 1953, *11*, 56–58.
8. Lucas, H. F. Improved low-level alpha scintillation counter for radon. *Rev. Sc. Instruments*, 1957, *28*, 680–683.
9. Medical uses of radium and radium substitutes. Public Health Service Publication No. 999-RH-16, July, 1965.
10. Morgan, J. E. Gas pressure in sealed radium containers. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1961, *85*, 949–954.
11. Peltier, S., and Duval, C. Sur la thermogravimetrie des precipites analytiques. IV. Dosage du baryum. *Anal. Chim. Acta*, 1947, *1*, 360–363.
12. Strominger, D., Hollander, J. M., and Seaborg, G. T. Table of isotopes. Part II. *Rev. Mod. Physics*, 1958, *30*, 585–904.
13. Van Roosenbeek, E., Shalek, R. J., and Moore, E. B. Explosion danger of medical radium sources. *Physics Med. & Biol.*, 1967, *12*, 121.
14. Wood, V. A. Collector. Collection of radium leak test articles. United States Public Health Service, MORP 68–1, March, 1968.

THE AMERICAN JOURNAL OF ROENTGENOLOGY RADIUM THERAPY AND NUCLEAR MEDICINE

Editor: TRAIAN LEUCUTIA, M.D.

Assistant to the Editor: KENNETH L. KRABBENHOFT, M.D.

Associate Editors: HARRY HAUSER, M.D., RUSSELL H. MORGAN, M.D., EDWARD B. D. NEUHAUSER, M.D.

Consulting Editorial Board: See front cover.

Published by: CHARLES C THOMAS, Publisher, 301–327 East Lawrence Avenue, Springfield, Illinois 62703.

Issued monthly. Annual subscription: United States, Mexico, Cuba, Central and South America, and Canada $20.00; other countries, $22.00. Current single numbers, $2.00. Advertising rates submitted on application. Editorial office, 401 Professional Building, Detroit, Michigan 48201. Office of publication, 301–327 East Lawrence Avenue, Springfield, Illinois 62703. Information of interest to authors and readers will be found on page ii.

AMERICAN ROENTGEN RAY SOCIETY

President: S. W. Brown, Augusta, Ga.; *President-Elect:* J. C. Cook, Detroit, Mich.; *1st Vice-President:* S. F. Ochsner, New Orleans, La.; *2nd Vice-President:* Herbert M. Stauffer, Philadelphia, Pa.; *Secretary:* T. F. Leigh, Emory University Clinic, Atlanta, Ga. 30322; *Treasurer:* C. B. Holman, Mayo Clinic, Rochester, Minn. 55901.

Executive Council: S. W. Brown, J. C. Cook, S. F. Ochsner, T. F. Leigh, C. B. Holman, T. M. Fullenlove, W. N. Hanafee, J. F. Roach, C. M. Nice, Jr., E. F. Lang, H. O. Peterson, C. A. Stevenson, C. A. Good, T. Leucutia, R. M. Scott, S. W. Nelson, R. L. Tondreau, W. B. Seaman, E. F. Van Epps, Chairman, Duke Univ., Durham, N. C., 27706.

Program Committee: T. F. Leigh, J. F. Roach, T. Leucutia, E. F. Lang, H. O. Peterson, W. N. Hanafee, S. W. Brown, E. F. Van Epps, J. C. Cook, Chairman, LL 14 Professional Plaza, 3790 Woodward Ave., Detroit, Mich. 48201.

Publication Committee: R. H. Greenspan, J. O. Reed, R. N. Cooley, P. A. Riemenschneider, J. F. Roach, Chairman, Albany, N. Y.

Finance and Budget Committee: R. L. Tondreau, W. B. Seaman, G. E. Sheline, J. M. Dennis, T. M. Fullenlove, Chairman, San Francisco, Calif.

Committee on Scientific Exhibits: R. E. Parks, R. G. Lester, W. N. Hanafee, Chairman, UCLA Medical Center, Los Angeles, Calif. 90024.

Advisory Committee on Education and Research: E. C. Klatte, A. R. Margulis, D. M. Witten, F. J. Bonte, C. M. Nice, Jr., Chairman, New Orleans, La.

Representatives on the American Board of Radiology: J. F. Roach, Albany, N. Y.; S. W. Nelson, Columbus, Ohio; and C. A. Stevenson, Spokane, Wash.

Director of Instruction Courses: H. O. Peterson, Minneapolis, Minn.; *Associate Director:* D. G. Mosser, Minneapolis, Minn.

Manager of the Annual Meeting: E. F. Lang, LL 14 Professional Plaza, 3790 Woodward Ave., Detroit, Mich. 48201.

Editor: T. Leucutia, 401 Professional Building, Detroit, Mich. 48201.

Representative on the Board of Chancellors of the American College of Radiology: S. F. Ochsner.

Seventieth Annual Meeting: Washington-Hilton Hotel, Washington, D. C., September 30–October 3, 1969.

AMERICAN RADIUM SOCIETY

President: Juan A. del Regato, Colorado Springs, Colo.; *President-Elect:* Fernando G. Bloedorn, Boston, Mass.; *1st Vice-President:* Clifford L. Ash, Toronto, Ont., Canada; *2nd Vice-President:* H. Peter Mueller, Boston, Mass.; *Secretary:* John V. Blady, The Parkway House, 2201 Benjamin Franklin Parkway, Philadelphia, Pa. 19130; *Treasurer:* James F. Nolan, 1407 South Hope St., Los Angeles, Calif. 90015.

Executive Committee: Justin J. Stein, Chairman, Los Angeles, Calif.; Juan A. del Regato; Fernando G. Bloedorn; Clifford L. Ash; H. Peter Mueller; John V. Blady; James F. Nolan; Milton Friedman; John L. Pool.

Scientific Program Committee: Juan A. del Regato, Chairman; Fernando G. Bloedorn, Vice-Chairman; Simon Kramer; Wm. E. Powers; Felix N. Rutledge; Jerome M. Vaeth.

Arrangements Committee: Luther W. Brady, Chairman, Philadelphia, Pa.; Gordon Verity, Chair man Designate; Larry McGowan; David Sklaroff; Antolin Raventos; James F. Nolan.

Publication Committee: Harry Hauser, Chairman, Cleveland, Ohio; Giulio J. d'Angio; William T. Moss.

Public Relations Committee: Antolin Raventos, Chairman; Robert Robbins; Harvey P. Groesbeck; Gordon Verity, *ex officio.*

Janeway Lecture Committee: Clifford L. Ash, Chairman, '69, Toronto, Ont., Canada; A. N. Arneson, '71; Milford D. Schulz, '73.

Representatives on the American Board of Radiology: Justin J. Stein, Los Angeles, Calif.; Ralph M. Scott, Louisville, Ky.; E. Richard King, Richmond, Va.

Liaison Representatives on the National Council on Radiation Protection and Measurements: Herbert M. Parker, Richland, Wash.; Marvin M. D. Williams, Rochester, Minn.

Representative on the Board of Chancellors of the American College of Radiology: Charles G. Stetson.

Fifty-first Annual Meeting: Bellevue Stratford Hotel, Philadelphia, Pa., April 28–30, 1969.

EDITORIAL

THE REYNOLDS HISTORICAL LIBRARY

ON A festive Sunday afternoon, February 2, 1958, "The Lawrence Reynolds Library" was dedicated with impressive ceremonies at the University of Alabama Medical Center in Birmingham.[1] Lawrence Reynolds, illustrious Editor of the JOURNAL for more than three decades,—great radiologist, eminent scholar, and above all famous bibliophile,—spent a lifetime in acquiring the rare books and private medical collections comprising this Library, which in filial devotion he donated to his Alma Mater and native State. Undoubtedly, it was the greatest moment of his life when, on that festive Sunday afternoon, he could say: "A diploma from the University of Alabama graced my wall for many years and every time I looked at it, I felt greatly indebted; so I am returning it to you with this handful of books." This "handful of books" at that time was a half-million dollar collection of early editions of works of some of the greatest medical and scientific pioneers of the fifteenth through the nineteenth centuries.

This unique Library is housed in a special wing which the University of Alabama has built as an extension of its new Medical Center Library. The collection is being continuously expanded and the name has been changed to "The Reynolds Historical Library."

Ten years later, the University of Alabama published a bibliography, in the format of an authoritatively conceived and beautifully composed Volume, titled *Rare Books and Collections of* THE REYNOLDS HISTORICAL LIBRARY: *A Bibliography*.[2] This Volume is affectionately dedicated to Howard Lamar Holley, Chairman of the Library and Editorial Committees of the University of Alabama, by Clifton K. Meador, John J. Sharry, and Sarah C. Brown, the other members of the Editorial Committee. The Volume contains 5,119 items, with a carefully compiled subject index and a name index (495 pages) and 28 magnificently reproduced illustrations of some of the most valuable items.

The motto of the Volume as quoted by Howard L. Holley in his chapter, "Lawrence Reynolds, M.D., The Bibliophile" is:

> *The General, the Statesman, the man of affairs, all pass away and are forgotten. But to have builded oneself into the structure of these undying institutions, to have aided the development of these priceless agencies of civilization, is to have lived not in vain, but is to have lived in perpetuity.*
> —Elihu Root

Dr. Holley concludes his chapter by saying: This cultural benefaction to the University of Alabama Medical Center and to this area will be felt as long as books remain a concern of civilized man—"because books have an ageless quality." Indeed, Dr. Lawrence Reynolds will live on through his books "in perpetuity."

In the Introduction Chapter to the compilation of the *Bibliography*, Martha Lou Thomas, Compiler, specifies the present status of the Library. She states that the Bibliography is now divided into five sections: incunabula, the main collection, the Daniel Drake collection, which was a

[1] LEUCUTIA, TRAIAN. The Lawrence Reynolds Library. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1958, 79, 726–727.

[2] HOLLEY, H. L., Chairman of the Library Committee of the University of Alabama and of the Editorial Committee. *Rare Books and Collections of* THE REYNOLDS HISTORICAL LIBRARY: *A Bibliography*. Published for the University of Alabama Medical Center Library, Birmingham, by the University of Alabama Press, University of Alabama, Birmingham, 1968, pp. 1–495, with 28 illustrations, some in color, and a photograph of Dr. Lawrence Reynolds.

special interest of Dr. Reynolds, the dental collection, and the manuscripts reflecting a broad interest in the Alabama Medical Center. For books published before 1600, complete title page transcriptions are given. After that date, the text gives only shorter titles and imprints, whenever possible to do so, without destroying the flavor of the book. The format of the book is not indicated after 1800. The terms, illustrations, maps, plates, portraits and tables cover all types of pictorial representations.

Some of the outstanding illustrations include: Anatomical manikins made in France, Italy and Germany in the 17th and 18th centuries; interior view of the Reynolds Library; illuminated first page of the 1478 edition of Celsus' *De Medicina*, Florence, Nicolaus Laurentii; pages 134–135 of Sir Thomas Browne's *Hydriotaphia* and *Cyrus-Garden* (urne-buriall), with marginal notes in the author's hand, London, 1658; the woodcut on the title page of Damian Carbon's *Libro del arte delas comadres*, Mallorca, 1541; Verso of leaf Aaii of the 1497 *Hortus Sanitatis*, Strassburg, Johann Prüss, 1497—and of the more recent ones: Letter from Florence Nightingale to Mrs. Schwabe, dated October 21, 1870; Letter from Louis Pasteur to M. Marchand on his dog's rabies, dated August 12, 1881; Letter from George Washington to his dentist, Dr. Baker of Philadelphia, dated April 11, 1783, and others.

Among the 5,119 items assiduously compiled there are many of interest to radiologists and associated scientists. William Gilbert, in 1600 published his epochal work *De magnete, magneticisque corporibus, et de magno magnete tellure; physiologia noua, plurimis & argumentis, & experimentis demonstrata*, which is considered a classic in the development of modern experimental science and laid the bases for the sciences of magnetism and electricity. This was followed by numerous fundamental publications by Benjamin Franklin (middle of the 18th century), Alessandro Volta (1769), Luigi Galvani (1786), Hans Christian Oersted (1820), André Marie Ampère (1820), Georg Simon Ohm (1827), Michel Faraday (1831–32), Joseph Henry (1839), and Sir William Crookes (1898). These important works and many others in the chain of development of the two sciences form an important part of the Library.

They lead to the vast collection of publications concerning directly the discovery, use, research and clinical application of the ionizing radiations, beginning with the turn of the century. There are more than 250 items dealing with electricity; 50 with magnetism; approximately 600 with roentgen rays, diagnostic and therapeutic; 30 with radium; 35 with radioactivity; 65 with physics; and there are 65 Nobel Prize papers. Among the rare items on radium is the Address, *The Discovery of Radium*, delivered by Madame M. Curie, at Vassar College on May 14, 1921, accompanied by an autographed photograph.

Many persons have contributed to the preparation of this *Bibliography*, including Miss Gertrude Annan, Librarian of the New York Academy of Medicine; Dr. Hubert Harper, Latin scholar and Literature Professor of the University of Alabama; Mr. Fant Thornley, Director of the Birmingham Public Library, and Mr. John D. Pittman.

Tinsley R. Harrison, in the chapter "Lawrence Reynolds, M.D., The Man" in describing his remarkably fruitful life and his many interests in other fields than radiology says: "The life of Dr. Reynolds may be compared to a diamond, not only in gleam and sparkle but also in number of facets." Dr. Harrison is the author of the inscription on the plaque at the entrance of the Reynolds Library, which reads:

> *Here are housed the books collected and loved by Lawrence Reynolds, physician, scholar and philanthropist. The official dedication ceremony of The Reynolds Library was held on February 2, 1958. But the more meaningful dedication will come from you who read these books. Each time one of you reaps from the great minds*

of the past the desire for finer achievement in your profession and nobler development of your own character, The Reynolds Library will have been rededicated.

This Journal, the official organ of the American Roentgen Ray Society and the American Radium Society, recognizes with a sense of deep reverence, that Lawrence Reynolds has brought renown to these Societies by the excellence and multitude of his scientific, philanthropic and above all bibliophilistic achievements.

Traian Leucutia, M.D.

NEWS ITEMS

NEW OFFICERS OF THE AMERICAN SOCIETY OF THERAPEUTIC RADIOLOGISTS

At the recent meeting of the American Society of Therapeutic Radiologists held at the Palmer House, Chicago, Illinois on December 3, 1968, in conjunction with the Fifty-fourth Annual Meeting of the Radiological Society of North America, the following officers were elected: Morton M. Kligerman, M.D., *President*; Simon Kramer, M.D., *President-Elect*; Gilbert H. Fletcher, M.D., *Chairman of Board of Directors*; Frank R. Hendrickson, M.D., *Member at Large*; Ralph M. Scott, M.D., *Member at Large*; Carl R. Bogardus, Jr., M.D., University of Oklahoma Medical Center, Oklahoma City, Oklahoma 73104, *Secretary*; and Howard B. Latourette, M.D., University of Iowa Medical Center, Iowa City, Iowa 52240, *Treasurer*.

The next meeting will be held in conjunction with the Fifty-first Annual Meeting of the American Radium Society, on April 29, 1969, at the Bellevue Stratford Hotel, Philadelphia, Pennsylvania 19102.

POSTGRADUATE COURSE IN NEURORADIOLOGY

A "Postgraduate Course in Neuroradiology" will be held March 10–14, 1969, at The Chase-Park Plaza Hotel, 212 North Kingshighway, St. Louis, Missouri 63108, under the chairmanship of Juan M. Taveras, M.D., Director of Edward Mallinckrodt Institute of Radiology, Washington University School of Medicine.

Supplementing the Washington University Faculty, the distinguished Guest Faculty includes: Giovanni Di Chiro, M.D., Head, Section on Neuroradiology, National Institute of Neurological Diseases and Blindness, National Institutes of Health, Clinical Center, Bethesda, Maryland; Norman E. Chase, M.D., Professor of Radiology, New York University School of Medicine, New York, New York; Torgny Greitz, M.D., Professor and Head, Neuroradiology Department, Karolinska Sjukhuset, Stockholm, Sweden; Bassett Kilgore, M.D., Associate Professor of Radiology, The University of Texas, Southwestern Medical School, Dallas, Texas; and D. Gordon Potts, M.D., Associate Professor of Radiology, Cornell University Medical College, New York, New York.

For further information please contact Juan M. Taveras, M.D., Director, Mallinckrodt Institute of Radiology, Washington University School of Medicine, 510 South Kingshighway, St. Louis, Missouri 63110.

MONTANA RADIOLOGICAL SOCIETY

The Symposium of the Montana Radiological Society will be held in Glacier National Park, July 23–25, 1969.

For reservations and further information please contact Colvin H. Agnew, M.D., Doctors' Building, 1231 N. 29th Street, Billings, Montana 59101.

POLYTECHNIC INSTITUTE OF BROOKLYN

The Polytechnic is planning to offer a 3 week intensive course in basic electronics and instrumentation techniques during late July and early August, 1969.

This will be a laboratory course designed for engineers, physical and biological scientists and science educators who must use instruments in their work, and it will be supported in part by the National Science Foundation under its College Teacher Programs.

For further information please write to Kenneth R. Jolls, 333 Jay Street, Brooklyn, New York 11201.

BOOK REVIEW

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

THE HUMAN BRONCHIAL CIRCULATION IN HEALTH AND DISEASE. By Leon Cudkowicz, M.D., M.R.C.P., F.A.C.P., Director, Cardio-Pulmonary Laboratory, Dalhousie University Faculty of Medicine, Halifax, Nova Scotia, Canada. Cloth. Pp. 424, with many illustrations. Price, $18.00. Williams & Wilkins Company, 428 E. Preston Street, Baltimore, Md. 21202, 1968.

Dr. Cudkowicz, Director of the Cardio-Pulmonary Laboratory of Dalhousie University in Halifax, has conducted investigation of the bronchial circulation for many years. His book presents the results of his work and brings together in easily accessible form much of the new information about the bronchial circulation.

Following an interesting historical account, the author reviews in detail the anatomy, physiology, and pharmacology of the bronchial circulation, including its embryology and its behavior in congenital abnormalities of the heart and pulmonary circulation.

Individual chapters discuss the bronchial circulation in lobar pneumonia, bronchiectasis and pulmonary infarction, pulmonary emphysema and chronic bronchitis, tuberculosis, neoplasms, collagen diseases, pulmonary hypertension, and bronchial circulation and innervation of the lung.

A chapter on finger clubbing and bronchial circulation is of particular interest in that the author has found indirect evidence for a causative humoral agent, which is probably destroyed in the lungs, but circulates generally when abnormal bronchopulmonary vascular anastomoses are present.

This is not a radiologic text and the bronchial angiograms, which are reproduced, are largely those of postmortem specimens. However, this work contains a great deal of important and useful information for any radiologist who wishes to undertake bronchial arteriography as a clinical examination.

The book also points out the many still unanswered questions relating to the role of the bronchial circulation in health and disease.

THEODORE E. KEATS, M.D.

BOOKS RECEIVED

PATHOLOGIE UND THERAPIE DER LYMPHOGRANULOMATOSE. By Prof. Dr. N. Ratkóczy. Cloth. Pp. 231 with 48 figures. Price, $10.00. Akadémiai Kiadó, Publishing House of the Hungarian Academy of Sciences, Budapest V Alkotmány U. 21, 1968.

SURGERY OF THE ADRENAL GLAND. By Frank Glenn, M.D., Lewis Atterbury Stimson Professor of Surgery Emeritus, Cornell University Medical College: Consultant to the Department of Surgery, the New York Hospital; Ralph E. Peterson, M.D., Professor of Medicine, Cornell University Medical College; Attending Physician, the New York Hospital; and Henry Mannix, Jr., M.D., Clinical Associate Professor of Surgery, Cornell University Medical College; Associate Attending Surgeon, the New York Hospital, New York, N. Y. Cloth. Pp. 179, with some illustrations. Price, $10.00. The Macmillan Company, 866 Third Avenue, New York, N. Y. 10022, 1968.

ENERGETICS AND MECHANISMS IN RADIATION BIOLOGY. Proceedings of a NATO Study Institute held in Portmeirion, April, 1967. Edited by Glyn O. Phillips, University of Salford, England. Cloth. Pp. 527, with many charts and some figures. Price, 130s ($22.50). Academic Press, Inc. (London) Ltd., Berkeley Square House, Berkeley Square, London WIX 6BA, England, 1968.

CARDIAC DIAGNOSIS. By Noble O. Fowler, M.D., Professor of Medicine; Director of Cardiac Research Laboratory, University of Cincinnati College of Medicine, Cincinnati, Ohio. Cloth. Pp. 736, with 503 illustrations. Price, $23.50. Hoeber Medical Division, Harper & Row, Publishers, 49 East 33rd Street, New York, N. Y. 10016, 1968.

AIDS TO ETHICS AND PROFESSIONAL CONDUCT FOR STUDENT RADIOLOGIC TECHNOLOGISTS. Second edition. By James Ohnysty, R.T.(A.R.R.T.), C.S.R.T., Department of Radiology, Saint Francis Hospital, Colorado Springs, Colorado. Cloth. Pp. 160. Price, $6.75. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill. 62703, 1968.

THE SPINE: A RADIOLOGICAL TEXT AND ATLAS. Third edition. By Bernard S. Epstein, M.D., Clinical Professor of Radiology, The Albert Einstein College of Medicine, New York; Director, Department of Radiology, The Long Island Jewish Hospital, New Hyde Park, New York; Radiologist-in-Chief, The Long Island Jewish Hospital—Queens Hospital Center Affiliation, New York,

N. Y. Cloth. Pp. 730, with 482 figures. Price, $35.00. Lea & Febiger, 600 Washington Square, Philadelphia, Pa. 19106, 1969.

Arthrography of the Knee Joint in Children. Roentgenologic Anatomy, Diagnosis and the Use of Multiple Discriminant Analysis. By Rasmus Stenström, the Aurora Hospital, Helsinki/Helsingfors, Finland. Acta Radiologica Supplementum 281. Paper. Pp. 86, with some illustrations. Price, Sw. Kr. 35;-. Acta Radiologica, Box 2052, Stockholm 2, Sweden, 1968.

Enzymhistochemische Untersuchungen am Carcinom des Corpus Uteri. Bibliotheca Gynaecologica, No. 49. Fortschritte der Geburtshilfe und Gynäkologie, Vol. 36. By A. Pfleiderer, Jr., Universitäts-Frauenklinik, Tübingen. Paper. Pp. 199, with 56 figures. Price, $12.95. S. Karger AG Basel. Distributed in USA by Albert J. Phiebig, P.O. Box 352, White Plains, N. Y. 10602, 1968.

Frontiers of Radiation Therapy and Oncology. Edited by Jerome M. Vaeth, San Francisco, Calif. Volume 3. The Relationship of Time and Dose in the Radiation Therapy of Cancer. Proceedings of the Third Annual San Francisco Cancer Symposium. Cloth. Pp. 249, with 114 figures. Price, $16.55. S. Karger AG Basel. In the USA, distributed by Albert J. Phiebig, P. O. Box 352, White Plains, N. Y. 10602, 1968.

Late Somatic Effects of Ionizing Radiation. By Charles D. Van Cleave, School of Medicine, University of North Carolina, Chapel Hill, N. C. Prepared under the auspices of the Division of Technical Information, United States Atomic Energy Commission. Paper. Pp. 310, with some figures. Price, $3.00. Clearinghouse for Federal Scientific and Technical Information, National Bureau of Standards, U. S. Department of Commerce, Springfield, Va. 22151, 1968.

Female Urology. By Houston S. Everett, M.D., Associate Professor of Gynecology and Obstetrics, Johns Hopkins University School of Medicine and Johns Hopkins Hospital, Baltimore, Md.; and John H. Ridley, M.D., F.A.C.O.G., Associate Professor of Clinical Gynecology and Obstetrics, Emory University School of Medicine; Gynecologist-in-Chief, Piedmont Hospital; Visiting Gynecologist, Grady Memorial Hospital and St. Joseph's Infirmary, Atlanta, Ga. Cloth. Pp. 240, with some illustrations. Price, $10.50. Hoeber Medical Division, Harper & Row, Publishers, 49 East 33rd Street, New York, N. Y. 10016, 1968.

A Review of the Nature and Uses of Examinations in Medical Education. By Josef Charvat, Chairman and Professor of Medicine, Charles University, Prague, Czechoslovakia; Christine McGuire, Chief, Evaluation Studies Section, Center for the Study of Medical Education, University of Illinois, College of Medicine, Chicago, Ill.; and Victor Parsons, Senior Lecturer in Medicine, King's College Hospital Medical School, University of London, England. Paper. Pp. 73. Price, $1.25. Public Health Papers, No. 36. World Health Organization, Geneva. The American Public Health Association, Inc., 1740 Broadway, New York, N. Y. 10019, 1968.

Proceedings in Echo-Encephalography. International Symposium on Echo-Encephalography, Erlangen, Germany, April 14–15, 1967. Edited by E. Kazner, Erlangen; W. Schiefer, Erlangen; and K. J. Zülch, Cologne. Cloth. Pp. 258, with 278 figures. Price, $17.00. Springer-Verlag New York Inc., 175 Fifth Avenue, New York, N. Y. 10010, 1968.

Quantitative Three-Dimensional Scintillography of the Stomach with Technetium (^{99m}Tc). By Kai Setälä, Max Siurala, Otto Nyyssönen and Erna Tarkiainen, the Department of Pathology and its Radiologic Laboratory, University of Helsinki, Finland. Acta Radiologica Supplementum 273. Paper. Pp. 44, with some illustrations. Price, Sw. Kr. 30;-. Acta Radiologica, Box 2052, Stockholm 2, Sweden, 1967.

Radiation-Induced Early Changes in Size and Vascularity of Cervical Carcinoma; A Colpophotographic and Clinical Study. By Per Bergsjø, Department of Gynaecology, the Norwegian Radium Hospital, Oslo, Norway. Acta Radiologica Supplementum 274. Paper. Pp. 86, with many figures. Price, Sw. Kr. 35;-. Acta Radiologica, Box 2052, Stockholm 2, Sweden, 1967.

The Parotid Gland in Subjects with and without Rheumatoid Arthritis; a Sialographic and Physiologic Study. By Sune Ericson, Departments of Oral Roentgenology and Otorhinolaryngology, Umeå University, Umeå, Sweden. Acta Radiologica Supplementum 275. Paper. Pp. 167, with some illustrations. Price, Sw. Kr. 40;-. Acta Radiologica, Box 2052, Stockholm 2, Sweden, 1968.

Anterior Teeth Relationship and Speech; Studies Using Cineradiography Synchronized with Speech Recording. By Rolf Jensen, Department of Orthodontics and Department of Odontological Roentgenology, School of Dentistry, Karolinska Institute, Stockholm. Acta Radiologica Supplementum 276. Paper. Pp. 70, with some illustrations. Price, Sw. Kr. 35;-. Acta Radiologica, Box 2052, Stockholm 2, Sweden, 1968.

Osteoarthrosis of the Knee: a Radiographic Investigation. By Sven Ahlbäck, Roentgen Department, St. Göran's Sjukhus, Stockholm. Acta Radiologica Supplementum 277. Paper. Pp. 71, with some illustrations. Price, Sw. Kr. 35;-. Acta Radiologica, Box 2052, Stockholm 2, Sweden, 1968.

SOCIETY PROCEEDINGS

MEETINGS OF RADIOLOGICAL SOCIETIES*

UNITED STATES OF AMERICA

AMERICAN ROENTGEN RAY SOCIETY
Secretary, Dr. Ted F. Leigh, Emory University Clinic, Atlanta, Ga. 30322. Annual Meeting: Washington-Hilton Hotel, Washington, D.C., September 30–October 3, 1969.

AMERICAN RADIUM SOCIETY
Secretary, Dr. John V. Blady, The Parkway House, 2201 Benjamin Franklin Parkway, Philadelphia, Pa. 19130. Annual meeting: Bellevue Stratford Hotel, Philadelphia, Pa., April, 28–30, 1969.

RADIOLOGICAL SOCIETY OF NORTH AMERICA
Secretary-Treasurer, Dr. Maurice Doyle Frazer, 1744 South Fifty-eighth St., Lincoln, Neb. Annual meeting: Palmer House, Chicago, Ill., November 30–December 5, 1969.

AMERICAN COLLEGE OF RADIOLOGY
Executive Director, William C. Stronach, 20 N. Wacker Drive, Chicago 6, Ill. Annual meeting: Regency Hyatt House, Atlanta, Ga., Feb. 18–22, 1969.

SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION
Secretary, Dr. Kenneth L. Krabbenhoft, Harper Hospital, Detroit, Mich. 48201. Annual meeting: New York, N. Y., July 13–17, 1969.

AMERICAN BOARD OF RADIOLOGY
Secretary, Dr. C. Allen Good. Correspondence should be directed to Kahler Center Building, Rochester, Minn. 55901.

The oral examinations will be held at the Pittsburgh Hilton Hotel, Pittsburgh, Pa., June 2–6, inclusive, 1969; and at the Statler Hilton Hotel, Dallas, Texas, Dec. 8–12, inclusive, 1969.

The written examination will be held in selected sites, Saturday, June 21, 1969.

The deadline for filing applications for any of the above three examinations was December 31, 1968.

AMERICAN ASSOCIATION OF PHYSICISTS IN MEDICINE
Secretary, Leonard Stanton, Hahnemann Medical College, 230 N. Broad St., Philadelphia, Pa. 19102.

AMERICAN SOCIETY OF THERAPEUTIC RADIOLOGISTS
Secretary, Dr. J. A. del Regato, Penrose Cancer Hospital, Colorado Springs, Colo. 80907.

AMERICAN SOCIETY FOR DIAGNOSTIC ULTRASOUND
Secretary, Dr. Charles C. Grossman, 552 N. Neville St., Pittsburgh, Pa. 15213.

AMERICAN SOCIETY OF NEURORADIOLOGY
Secretary-Treasurer, Dr. Alan E. Zimmer, Danbury, Conn. 06810.

TWELFTH INTERNATIONAL CONGRESS OF RADIOLOGY
President, Dr. Kempo Tsukamoto, 9-1, 4-chome, Angewa, Chiba, Japan. Meeting: Hotel New Otani, Tokyo, Japan, Oct. 6–11, 1969.

TENTH INTER-AMERICAN CONGRESS OF RADIOLOGY
Counselor for the United States, Dr. Juan A. del Regato, Penrose Cancer Hospital, 2215 North Cascade Ave., Colorado Springs, Colo. 80907.
President, Dr. Juan A. del Regato, Colorado Springs, Colo., USA.
Secretary, Dr. F. Bloedorn, Boston, Mass., USA.
Meeting: San Juan, Puerto Rico, 1971.

INTER-AMERICAN COLLEGE OF RADIOLOGY
President, Dr. Oscar Soto, H. Urteaga 480, Lima, Perú.

ALABAMA RADIOLOGICAL SOCIETY
Secretary, Dr. Walter Brower, Birmingham, Ala. Meets time and place of Alabama State Medical Association.

ALASKA RADIOLOGICAL SOCIETY
Secretary, Dr. Bruce C. Wright, Providence Hospital, Anchorage, Alaska. Meets third Wednesday each month.

ARIZONA RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Robert E. Steyskal, 550 W. Thomas Rd., Phoenix, Ariz. 85013. Two regular meetings a year. Annual meeting at time and place of State Medical Association and interim meeting six months later.

ARKANSAS CHAPTER OF AMERICAN COLLEGE OF RADIOLOGY
Secretary-Treasurer, Dr. Wilma C. Diner, Univ. of Arkansas Medical Center, Little Rock, Ark. 72201.

ARKANSAS RADIOLOGICAL SOCIETY
Secretary, Dr. Charles W. Anderson, 1108½ Poplar, Pine Bluff, Ark. Meets every three months and also at time and place of State Medical Association.

ASSOCIATION OF UNIVERSITY RADIOLOGISTS
Secretary-Treasurer, Dr. Alexander Gottschalk, University of Chicago Medical School, Chicago, Ill. 60637. Annual Meeting: University of California, San Francisco, May 7–10, 1969.

ATLANTA RADIOLOGICAL SOCIETY
Secretary, Dr. Donald R. Rooney, Burnt Hickory Road, Marietta, Ga. Meets monthly except during three summer months, on third Tuesday, at the Academy of Medicine, Atlanta, Ga., at 8:00 P.M.

BAVARIAN-AMERICAN RADIOLOGIC SOCIETY
Advisor, Colonel Paul E. Sieber. *Secretary*, Major Peter B. Riesz, USAH Bad Cannstatt, APO 09154, New York, N. Y. Meets quarterly.

BLOCKLEY RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. R. John Gould, 41 Lombardy Rd., Drexel Hill, Pa. 19026.

BLUEGRASS RADIOLOGICAL SOCIETY
Secretary-Treasurer, Joseph A. Sayeg, Ph.D., Radiation Physicist, University of Kentucky, Lexington, Kentucky 40506. The Society meets once each month during the school year.

BROOKLYN RADIOLOGICAL SOCIETY
Secretary, Dr. Coleman H. Rosenberg, 81–10 Chevy Chase St., Jamaica, N.Y. 11432. Meets first Thursday of each month, October through June.

BUFFALO RADIOLOGICAL SOCIETY
Secretary, Dr. Courtland Van Deusen, 817 Main St., Niagara Falls N. Y. 14301. Meets second Monday evening each month, October to May inclusive., at University Club.

CALIFORNIA RADIOLOGICAL SOCIETY
Secretary-Treasurer: Dr. Leroy K. Mills, 3157 Oakcliff Circle, Carmichel, Calif. 95608. Meets annually during meeting of California Medical Association.

CATAWBA VALLEY RADIOLOGICAL SOCIETY
Secretary, Dr. Emmett R. White, P. O. Box 303, Rutherford College, N. C. 28671. Meets every Friday, Dept. of Radiology, Valdese General Hosp., Valdese, N. C., at 12:00 NOON.

CENTRAL NEW YORK RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. George, Mitchell, Radiology Department, Syracuse Memorial Hospital, Syracuse, N. Y. 13210. Meets first Monday each month, October through May.

CENTRAL OHIO RADIOLOGICAL SOCIETY
Secretary, Dr. Ollie E. Southard, 2787 Tudor Rd., Columbus, O. 43209. Meets second Thursday in October, November, January, and March 15 and May 19 at Fort Hayes Hotel, Columbus, Ohio.

* Secretaries of societies are requested to send timely information promptly to the Editor.

Chicago Roentgen Society
Secretary-Treasurer, Dr. Howard C. Burkhead, 2650 Ridge Ave., Evanston, Ill. 60202. Meets third Wednesday of each month, October to April, except December, at the University Club of Chicago.

Cleveland Radiological Society
Secretary-Treasurer, Dr. James Farmer, 18869 Canyon Rd. Fairview Park, Ohio 44126. Meetings at 7:00 P.M. on fourth Monday of October, November, January, February, March and April.

Colorado Radiological Society
Secretary, Dr. Charles E. Seibert, Department of Radiology, Swedish Hospital, 501 E. Hampton, Englewood, Colo. 80110. Meets third Friday of each month at Denver Athletic Club from September through May.

Connecticut Valley Radiologic Society
Secretary, Dr. William W. Walthall, Jr., 130 Maple St., Springfield, Mass. Meets in April and October.

Dallas-Fort Worth Radiological Society
Secretary-Treasurer, Dr. R. W. Perrin, P.O. Box 5999, Dallas, Texas 75222. Meets the 3rd Monday of every month at 6:30 P.M., at the Cibola Inn, Arlington, Texas.

Detroit Roentgen Ray Society
Secretary, Dr. David P. Corbett, Harper Hospital, Detroit, Mich. 48201. Meets monthly, first Thursday, October through May, at David Whitney House, 1010 Antietam, at 6:30 P.M.

East Bay Radiological Society
Secretary, Dr. Allen B. Freitag, 411 30th Str., Oakland, Calif. 94609. Meets first Thursday each month, Oct. through May, at University Club, Oakland, Calif.

East Tennessee Radiological Society
Secretary-Treasurer, Dr. Eberhard F. Besemann, Baroness Erlanger Hospital, Chattanooga, Tenn. 37403. Meets in January and September.

Florida Radiological Society
Secretary, Dr. Robert H. Nickau, Good Samaritan Hospital, West Palm Beach, Fla. 33402. Meets twice annually, in the spring with the annual State Society Meeting and in the fall.

Florida West Coast Radiological Society
Secretary-Treasurer, Dr. Allen L. Sheer, University Community Hospital, 13505 N. 31st St., Tampa, Fla. 33612. Meets in January, March, May, July, September and November.

Georgia Radiological Society
Chapter of the American College of Radiology
Secretary, Dr. Walker Harris, The Medical Center, Columbus, Georgia 31902. Meets in spring and fall at Annual State Society Meeting.

Greater Cincinnati Radiological Society
Secretary-Treasurer, Dr. Owen L. Brown, 2421 Auburn Ave., Cincinnati, Ohio 45219.

Greater Louisville Radiological Society
Secretary-Treasurer, Dr. L. D. LeNeave, 315 E. Broadway, Louisville, Ky. 40202. Meets monthly.

Greater Miami Radiological Society
Secretary-Treasurer, Dr. Sylvan H. Sarasohn, North Miami General Hospital, 1701 Northeast 127th St., North Miami, Fla. 33161. Meets monthly, third Wednesday at 8:00 P.M. at Jackson Memorial Hospital, Miami, Fla.

Greater St. Louis Society of Radiologists
Secretary-Treasurer, Dr. Roland P. Ernst, 3720 Washington Ave., St. Louis, Mo. 63108.

Hawaii Radiological Society
Secretary-Treasurer, Dr. Thomas C. Brown, 1697 Ala Moana Blvd., Honolulu, Hawaii 96815. Meets third Monday of each month at 7:30 P.M.

Health Physics Society
Secretary, R. J. Augustine, National Center for Radiologic Health, 1901 Chapman Ave., Rockville Md. 20852.

Houston Radiological Society
Secretary, Dr. Eleanor Montague, 6516 Bertner, Houston, Tex. 77025. Meets fourth Monday of each month, except June, July, August and December, at 6:00 P.M., at 103 Jesse H. Jones Library Building, Texas Medical Center, Houston, Tex. 77025.

Idaho State Radiological Society
Secretary, Dr. George H. Harris, Bannock Memorial Hospital, Pocatello, Idaho. Meets in the spring and fall.

Illinois Radiological Society, Inc.
Secretary, Dr. C. R. Markivee, 674 North Seminary St., Galesburg, Ill. 61401. Meets in the spring and fall.

Indiana Roentgen Society, Inc.
Secretary, Dr. Edwin F. Koch, Jr., 915 University Ave., Muncie, Ind. 47303. Meets first Sunday in May and during fall meeting of Indiana State Medical Association.

Iowa Radiological Society
Secretary-Treasurer, Dr. J. H. Lohnes, 1948 First Ave., N.E., Cedar Rapids, Iowa 52402. Luncheon and business meeting during annual session of Iowa State Medical Society. The scientific section is held in the autumn.

Kansas Radiological Society
Secretary-Treasurer, Dr. Robert C. Lawson, 310 Medical Arts Bldg., 10th and Horne, Topeka, Kan. Meets in spring with State Medical Society and in winter on call.

Kentucky Chapter, American College of Radiology
Secretary-Treasurer, Dr. Ralph C. Quillin, 1221 S. Broadway, Lexington, Ky. 40504. Meets in April and September.

Kings County Radiological Society
Secretary, Dr. Sidney Hendler, 1880 Ocean Ave., Brooklyn 30, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

Knoxville Radiological Society
Secretary, Dr. Clifford L. Walton, Blount Professional Bldg., Knoxville 20, Tenn. Meetings are held the third Monday of every other month at the University of Tennessee Memorial Research Center and Hospital.

Long Island Radiological Society
Secretary, Dr. Robert J. Hochstim, 1200 Stewart Ave., Garden City, N. Y. 11533. Meets monthly.

Los Angeles Radiological Society
Secretary, Dr. John L. Gwinn, Childrens Hospital of Los Angeles, 4650 Sunset Blvd., Los Angeles, Calif. 90027. Meets second Wednesday of month in September, November, January, April and June at Los Angeles County Medical Association Building, Los Angeles, Calif.

Louisiana-Texas Gulf Coast Radiological Society
Secretary-Treasurer, Dr. Edward A. Sheldon, 109 Doctors Bldg., Beaumont, Texas 77701.

Maine Radiological Society
Secretary-Treasurer, Dr. Robert A. Bearor, Maine Medical Center, Portland, Maine 04102. Meets in June, September, December and April.

Maryland Radiological Society
Secretary, Dr. Henry Startzman, Medical Arts Building, Baltimore, Md.

Massachusetts Radiological Society
Secretary, Dr. Jerome H. Shapiro, Department of Radiology, Boston City Hospital, 818 Harrison Ave., Boston, Mass. 02118.

Memphis Roentgen Society
Secretary-Treasurer, Dr. Webster Riggs, Jr., The University of Tennessee College of Medicine, Department of Radiology, Walter F. Chandler Bldg., 865 Jefferson Ave., Memphis, Tenn. 38103. Meets first Monday of each month at John Gaston Hospital.

Miami Valley Radiological Society
Secretary, Dr. Darwood B. Hance, Reid Memorial Hospital, Richmond, Indiana. Meets third Thursday of fall, winter and spring months at 7:30 P.M. at Miami Valley Hospital, Dayton, Ohio.

Mid-Hudson Radiological Society
Secretary-Treasurer, Dr. Herbert S. Berlin, Hopewell Junction, N. Y. Meets 7:00 P.M., first Wednesday of each month, September to May.

Milwaukee Roentgen Ray Society
Secretary-Treasurer, Dr. James E. Bell, 8700 W. Wisconsin Ave., Milwaukee, Wis. 53213. Meets monthly on fourth Monday, October through May, at University Club.

Minnesota Radiological Society
Secretary-Treasurer, Dr. Warren L. Kump, 4243 Glenwood Ave., Minneapolis, Minn. 55422. Meets twice annually, fall and winter.

Mississippi Radiological Society
Secretary-Treasurer, Dr. Dan T. Keel, Jr., 504 Chippewa St., Brookhaven, Miss. Meets third Thursday of each month at the Heidelberg Hotel, Jackson, at 6:00 P.M.

Missouri Radiological Society
Secretary-Treasurer, Dr. Arthur A. Porporis, 100 N. Euclid Ave., St. Louis, Mo. 63108.

Montana Radiological Society
Secretary, Dr. Colvin H. Agnew, Doctors' Building, 1231 N. 29th Street, Billings, Montana 59101. Meets in Glacier National Park, July 23–25, 1969.

Nebraska State Radiological Society
Secretary-Treasurer, Dr. Otto A. Troester, 924 Sharp Building, Lincoln, Nebraska 60508. Meets third Wednesday of each month at 6 P.M. in Omaha or Lincol ε

Nevada Radiological Society
Secretary, Dr. William G. Arbonies, Department of Radiology, St. Mary's Hospital, Reno, Nev.

New England Roentgen Ray Society
Secretary, Dr. Morris Simon, 330 Brookline Ave., Boston, Mass. 02115. Meets third Friday of each month, October through May, at The Longwood Towers, 20 Chapel Street, Brookline, Mass., at 4:30 P.M. The Annual Meeting will be held May 24 and 25, 1969, at the Hotel Belmont, West Harwich by-the-sea, Cape Cod, Mass. The guest speaker, Dr. Lucy Frank Squire, will present the Twenty-fifth George W. Holmes Lecture.

New Hampshire Roentgen Ray Society
Secretary, Dr. Paul Y. Hasserjian, 1470 Elm St., Manchester, N. H. Meets four to six times yearly.

New Mexico Association of Radiologists
Secretary-Treasurer, Dr. Justin J. Wolfson, Department of Radiology, Bernalillo County-Indian Hospital, Albuquerque, New Mexico.

New Mexico Society of Radiologists
Secretary, Dr. Phil Fox, Albuquerque, New Mexico. Four meetings annually, three held in Albuquerque, N. M., and one held at time and place of New Mexico State Medical Society annual meeting.

New York Roentgen Society
Secretary-Treasurer, Dr. Samuel H. Madell, 1 E. 82nd St New York, N. Y. 10024. Meets monthly on third Monday at the New York Academy of Medicine at 4:30 P.M.

New York State Chapter of the American College of Radiology, Inc.
Secretary-Treasurer, Dr. John W. Colgan, 273 Hollywood Ave., Rochester, N. Y., 14618.

North Carolina Chapter of ACR.
Secretary-Treasurer, Dr. Ira Bell, Hickory, N. C.

North Carolina Radiological Society
Secretary, Dr. E. H. Schultz, North Carolina Memorial Hospital, Chapel Hill, N. C. Meets in the spring and fall each year.

North Dakota Radiological Society
Secretary, Dr. A. Ohrt, 408 Medical Arts Bldg., Fargo, N. D. 58102. Meets at time of State Medical Association meeting. Other meetings arranged on call of the President.

North Florida Radiological Society
Secretary, Dr. Charles H. Newell, 800 Miami Road, Jacksonville 7, Fla. Meets quarterly in March, June, September and December.

Northeastern New York Radiological Society
Secretary, Dr. Herbert F. Reilly, Jr., 12 Sandalwood Rd., Scotia, New York 12302. Meets in Albany area on third Wednesday of October, November, March, April, and May.

Northern California Radiological Society
Secretary-Treasurer, Ivan D. Siddons, 3701 J. St., Suite 106, Sacramento, Calif. 95816. Meets fourth Monday of Sept., Nov., Jan., March and May at the Sutter Club in Sacramento.

Northwestern Ohio Radiological Society
Secretary, Dr. Vito J. Zupa, Mercy Hospital, Department of Radiology, Toledo, Ohio.

Ohio State Radiological Society
Secretary, Dr. Robert D. Berkebile, Elyria Memorial Hospital, Elyria, Ohio 44035.

Oklahoma State Radiological Society
Secretary, Dr. Donald F. Mauritson, 100 Utica Square Med. Center, Tulsa, Okla. 74114. Meets in January, May and October.

Orange County Radiological Society
Secretary, Dr. Richard Simpson, Hoag Memorial Hospital, 301 Newport Ave., Newport Beach, California. Meets on fourth Tuesday of the month, excluding June, July, August, and December, at the Orange County Medical Association Bldg. Orange, Calif.

Oregon Radiological Society
Secretary-Treasurer, Dr. Clinton B. Sayler, 214 Medical Dental Bldg., Portland, Oregon 97205. Meets on second Wednesday of month, October through April, at the University Club, Portland, Ore.

Orleans Parish Radiological Society
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans, La. 70113. Meets second Tuesday of each month.

Pacific Northwest Radiological Society
Secretary-Treasurer, Dr. Marvin Wallace, 555 108th Ave. N. E., Bellevue, Washington 98004.

Pennsylvania Radiological Society
Secretary, Dr. Theodore A. Tristan, Harrisburg, Polyclinic Hosp., Harrisburg, Pa. 17105.

Philadelphia Roentgen Ray Society
Secretary, Dr. C. Jules Rominger, Misericordia Hospital, 54th St. and Cedar Ave., Philadelphia, Pa. 19143. Meets first Thursday of each month at 5 P.M., from October to May in Thompson Hall, College of Physicians.

Pittsburgh Roentgen Society
Secretary, Dr. Edward R. Seitz, 601 Jenkins Bldg., Pittsburgh, Pa. 15222. Meets second Wednesday of month, October through June, at Park Schenley Restaurant.

Radiation Research Society
Secretary-Treasurer, Dr. Gail D. Adams, Dept. of Radiology, Univ. of Oklahoma Medical Center, Oklahoma City, Oklahoma 73104. Annual Meeting: Netherland Hilton Hotel, Cincinnati, Ohio, May 18–22, 1969.

Radiological Society of Connecticut, Inc.
Secretary-Treasurer. Dr. Henry J. Fox, 10 Washington Ave., Bridgeport, Conn. Meetings are held quarterly.

Radiological Society of Greater Cincinnati
Secretary-Treasurer, Dr. Donald E. Gunderson, 3553 Bayard Dr., Cincinnati, Ohio 45208. Meets first Monday of each month at Cincinnati Academy of Medicine.

Radiological Society of Greater Kansas City
Secretary, Dr. J. Stewart Whitmore, 1010 Rialto Bldg., Kansas City, Mo. Meets last Friday of each month.

Radiological Society of Kansas City
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

Radiological Society of Louisiana
Secretary, Dr. Lester W. Eavenson, 2700 Napoleon Ave., New Orleans 15, La. Meets semiannually, during Louisiana State Medical Society meeting and 6 months later.

Radiological Society of New Jersey
Secretary, Dr. John W. Marquis, 12 Hawthorne Ave., East Orange, N. J. 07018. Meets in Atlantic City at time of State Medical Society meeting and in October or November in Newark, N. J.

Radiological Society of Rhode Island
Secretary-Treasurer, Dr. John M. Vesey, 1196 Elmwood Ave., Cranston, R. I.

Radiological Society of South Dakota
Secretary-Treasurer, Dr. Donald J. Peik, 303 S. Minnesota Ave., Sioux Falls, S. D.

Radiological Society of Southern California
Secretary-Treasurer, Dr. Robert G. Williams, The Santa Barbara Medical Clinic, P.O. Box 1200, Santa Barbara, Calif. 93102. Meets three times a year, usually October, February and May.

Radiological Society of the State of New York
Secretary-Treasurer, Dr. John W. Colgan, 273 Hollywood Ave., Rochester, N. Y. 14618.

Redwood Empire Radiological Society
Secretary, Dr. Lee F. Titus, 164 W. Napa St., Sonoma, Calif. Meets second Monday every other month.

Richmond County Radiological Society
Secretary, Dr. W. F. Hamilton, Jr., University Hospital, Augusta, Ga. Meets first Thursday of each month at various hospitals.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. Kenneth E. Robinson, Rochester General Hospital, 1425 Portland Ave., Rochester, N. Y. 14621. Quarterly meetings on the call of the President, at the Rochester Academy of Medicine.

Rocky Mountain Radiological Society
Secretary-Treasurer, Dr. Robert W. Lackey, 4200 E. Ninth Ave., Denver, Colo. 80220. Annual meeting: Brown Palace Hotel, Denver, Colo., Aug. 21–23, 1969.

San Antonio-Military Radiological Society
Secretary, Dr. Hugho F. Elmendorf, Jr., 730 Medical Arts Bldg., San Antonio 5, Tex. Meets third Wednesday of each month in Fort Sam Houston Officer's Club at 6:30 P.M.

San Diego Radiological Society
President-Secretary, Charles R. Henkelmann, 3909 Palm Drive, Bonita, Calif. 92002. Meets first Wednesday of each month at the Town & Country Motel.

San Francisco Radiological Society
Secretary-Treasurer, Dr. Warren M. Russell, Franklin Hospital, Castro & Duboce, San Francisco, Calif. 94114. Meets quarterly at various hospitals (contact Secretary).

Santa Clara County Radiological Society
Secretary, Dr. John J. Berg, 45 So. 17th Street, San Jose Calif. 95112. Meets monthly at the Santa Clara County Medical Association Bldg., 700 Empey Way, San Jose, Calif.

Section on Radiology, California Medical Association
Secretary, Dr. William H. Graham, 630 East Santa Clara St., San Jose, Calif.

Section on Radiology, Medical Society of the District of Columbia
Secretary-Treasurer, Dr. Louis Wener, Cafritz Memorial Hosp., 1310 Southern Ave., S.E., Washington, D. C. 20032. Meets at Medical Society Library, third Wednesday of January, March, May and October at 8:00 P.M.

Section on Radiology, Southern Medical Association
Secretary, Dr. Phillip W. Voltz, Jr., 120 Medical Professional Bldg., San Antonio, Texas 78212. Annual meeting: To be announced.

Section on Radiology, Texas Medical Association
Secretary, Dr. George F. Crawford, St. Elizabeth Hospital, Beaumont, Tex. Meets annually with the Texas Medical Association.

Shreveport Radiological Club
Secretary, Dr. W. R. Harwell, 608 Travis St., Shreveport, La. Meets monthly on third Wednesday at 7:30 P.M., September to May inclusive.

Society for Pediatric Radiology
Secretary, Dr. John L. Gwinn, Children's Hospital, 4614 Sunset Blvd., Los Angeles 27, Calif. Annual meeting: Washington-Hilton Hotel, Washington, D.C., September 29, 1969.

Society of Nuclear Medicine
Secretary, Mr. C. Craig Harris, Oak Ridge National Laboratories, Oak Ridge, Tenn. *Administrator*, Mr. Samuel N. Turiel, 430 N. Michigan Ave., Chicago 11, Ill. Annual meeting Jung Hotel, New Orleans La., June 22–28, 1969.

South Bay Radiological Society
Secretary, Dr. Emerson C. Curtis, University Dr., Menlo Park, Calif. 94025. Meets second Wednesday of each month.

South Carolina Radiological Society
Secretary, Dr. George W. Brunson, 1406 Gregg St., Columbia, S. C. Annual meeting (primarily business) in conjunction with the South Carolina Medical Association meeting in May. Annual fall scientific meeting at time and place designated by the president.

South Dakota Radiological Society
Secretary, Dr. Donald J. Peik, 1417 S. Minnesota Ave., Sioux Falls, S. Dak. Meets in spring with State Medical Society and in fall.

Southern California Radiation Therapy Society
Secretary-Treasurer, Dr. Aaron G. Fingerhut, 1000 W. Carson St., Torrance, Calif. 90502. Meets quarterly.

Southern Radiological Conference
Secretary-Treasurer, Dr. Marshall Eskridge, Mobile Infirmary, P.O. Box 4097, Mobile, Ala. 36604. Annual meeting: Grand Hotel, Pointe Clear, Ala. 36564, Jan. 31–Feb. 2, 1969.

Southwestern Radiological Society
Secretary, John M. McGuire, 904 Chelsea, El Paso, Tex. Meets last Monday of each month at 6:30 P.M. in the Paso del Norte Hotel.

Tennessee Radiological Society
Secretary-Treasurer, Dr. Marion E. Spurgeon, Memorial Hosp., Clarksville, Tenn. 37040. Meets annually at the time and place of the Tennessee State Medical Association meeting.

Texas Radiological Society
Secretary, Dr. Herman C. Sehested, 815 Medical Arts Bldg., Fort Worth 2, Tex. Annual meeting to be announced.

Tri-State Radiological Society
Secretary, Dr. John H. Marchand, Jr., Methodist Hospital, Henderson, Ky. Meets third Wednesday of Oct., Jan., March and May, 8:00 P.M., Elks Club in Evansville, Ind.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7:00 P.M. at University Hospital, Ann Arbor Mich.

Upper Peninsula Radiological Society
Secretary, Dr. A. Gonty, Menominee, Mich. Meets quarterly.

Utah State Radiological Society
Secretary-Treasurer, Dr. Leon M. Neal, St. Benedict's Hospital, 3000 Polk Ave., Ogden, Utah 84403. Meets fourth Wednesday in January, March, May, September and November at Holy Cross Hospital.

Vermont Radiological Society
Secretary, Dr. John R. Williams, 160 Allen St., Rutland, Vt.

Virginia Radiological Society
Secretary-Treasurer, Dr. K. Kenneth Wallace Jr., Norfolk, Va.

Washington State Radiological Society
Secretary-Treasurer, Dr. Paul S. Paulson, 1001 Broadway, Seattle, Washington 98122. Meets quarterly.

West Virginia Radiological Society
Secretary-Treasurer, Dr. George G. Green, Department of Radiology, W. Va. Univ. Medical Center, Morgantown, W. Va. 26506. Meets concurrently with Annual Meeting of West Virginia State Medical Society; other meetings arranged by program committee.

Westchester County Radiological Society
Secretary, Dr. Arnold Gerson, Medical Arts Bldg., Mt.

Vernon, N. Y. Meets on third Tuesday of January and October and on two other dates.

Wisconsin Radiological Society
Secretary-Treasurer Dr. Robert E. Douglas, 117 N. Commerical St., Neenah, Wis. 54956. Meets twice a year, May and September.

Wyoming Radiological Society
Secretary, Dr. J. D. Grant, Memorial Hosp., Sheridan, Wyo. Meets in fall with State Medical Society and in spring on call of President.

Cuba, Mexico, Puerto Rico and Central America

Asociación Costariccense de Radiología
Secretary, Dr. Jorge Vargas Segura, Apartado 5367, San José, Costa Rica.

Asociación de Radiólogos de Centro America y Panamá. Comprising: Guatemala, El Salvador, Honduras, Nicaragua, Costa Rica and Panamá.
Secretary-General, Dr. Roberto Calderón, Calle Central Oeste No. 218, Managua, Nicaragua, Central America. Meets annually in a rotating manner in the six countries.

Sociedad de Radiología de El Salvador
Secretary, Dr. Julio Astacio, 5a Av. Nte. No. 434, San Salvador, Rep. El Salvador.

Sociedad de Radiología de Guatemala
Secretary, Dr. Carlos E. Escobar, 9ª. Calle A 0-05, Zona 1, Guatemala.

Sociedad de Radiología y Fisioterapía Cubana
Secretary, Dr. Miguel A. García Plasencia, Hospital Curie, 29 y F, Vedado, Habana, Cuba Meets monthly at Curie Hospital.

Sociedad Mexicana de Radiología, A.C.
Coahuila No. 35, México 7, D. F.
Secretary-General, Dr. Ramón Ruenes.
Meets first Monday of each month.

Asociación Puertorriqueña de Radiología
Secretary, Dr. R. B. Díaz Bonnet, Suite 504, Professional Bldg., Santurce, Puerto Rico.

Sociedad Radiológica Panameña
Secretary, Dr. L. Arrieta Sánchez, Apartado No. 6323, Panamá, R. de P. Meets monthly in a department of radiology of a local hospital chosen at preceding meeting.

Sociedad Radiológica de Puerto Rico
Secretary, Dr. Felipe N. de Jesús, Apt. 9387, Santurce, Puerto Rico. Meets second Thursday of each month at 8:00 P.M. at the Puerto Rico Medical Association Bldg. in San Juan.

British Commonwealth of Nations

Association of Radiologists of the Province of Quebec
Secretary, Dr. R. Robillard, Notre-Dame Hospital, 1560 Sherbrooke St., East, Montreal, Que., Canada. Meets four times a year.

British Institute of Radiology
Honorary Secretary, Dr. G. H. du Boulay, 32 Welbeck St., London, W. 1, England. Meets monthly from October until May.

Canadian Association of Physicists, Division of Medical and Biological Physics.
Honorary Secretary-Treasurer, Paul M. Pfalzner, Department of Therapeutic Radiology, University of Western Ontario, London, Ontario, Canada.

Edmonton and District Radiological Society
Secretary, J. D. R. Miller, M.B., University of Alberta Hospital, Edmonton, Alberta, Canada. Meets third Thursday of each month October to May, except December, at various Edmonton Hospitals.

Faculty of Radiologists
Honorary Secretary, Dr. J. N. Pattinson, 47 Lincoln's Inn Fields, London, W.C.2, England.

Faculty of Radiologists, Royal College of Surgeons in Ireland
Registrar, Dr. H. O'Flanagan, F.R.C.P.I., D.P.H., 123 St. Stephens Green, Dublin 2, Ireland.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets third Friday each month at 4:45 P.M. at the Royal Society of Medicine, 1 Wimpole St., London, W. 1, England.

Canadian Association of Radiologists
Honorary Secretary-Treasurer, Dr. Maurice Dufresne, *Associate Honorary Secretary-Treasurer*, Dr. F. Robert MacDonald, 1555 Summerhill Ave., Montreal 25, Que., Canada. Annual Meeting at the Hotel Vancouver, Vancouver, B.C., March 10–14, 1969.

Montreal Radiological Study Club
Secretary, Dr. Leonard Rosenthall, Montreal General Hospital, Montreal, Que., Canada. Meets first Tuesday evening, October to April.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Société Canadienne-Française de Radiologie
Secretary General, Dr. Guy Duckett, 1385 est, rue Jean Talon, Montréal P.Q., Canada. Meets every third Tuesday from October to April. Annual Meeting: Nov. 13–15, 1969.

Toronto Radiological Society
Secretary, Dr. George Wortzman, Toronto General Hosp., Toronto 12, Ont., Canada. Meets second Monday of each month, September through May.

College of Radiologists of Australasia
Honorary Secretary, Dr. T. P. Loneragan, c/o British Medical Agency, 135 Macquarie St., Sydney, N.S.W., Australia.

South America

Asociación Argentina de Radiología
Secretary, Dr. Lidio G. Mosca, Avda. Gral. Paz 151, Córdoba, Argentina. Meetings held monthly.

Ateneo de Radiologia
Secretary, Dr. Victor A. Añaños, Instituto de Radiologia, Santa Fe 3100, Rosario, Argentina. Meets monthly on second and fourth Fridays at 7:00 P.M. in the Hospital Nacional de Centenario, Santa Fe 1300, Rosario.

Colégio Brasileiro de Radiologia
Secretary-General, Dr. Miguel Mario Céntola, Caixa Postal 5984, São Paulo, Brazil.

Sociedad Argentina de Radiologia
Secretary-General, Dr. Oswaldo E. Zerbo, Santa Fe 1171, Buenos Aires. Meetings are held monthly.

Sociedad Boliviana de Radiología
Secretary, Dr. Javier Prada Méndez. Casilla 1182, La Paz, Bolivia. Meets monthly. General assembly once every two years.

Sociedade Brasileira de Radiologia
Secretary, Dr. Armando Rocha Amoédo, Cxa Postal 1532, Rio de Janeiro, Brazil. General Assembly meets every two years in December.

Sociedade Brasileira de Radioterapia
Secretary, Dr. Oscar Rocha von Pfuhl, Av. Brigadeiro Luiz Antonio, 644, São Paulo, Brazil. Meets monthly on second Wednesday at 9:00 P.M. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

Sociedad Chilena de Radiología
Secretary, Dr. Manuel Concha, Casilla 13426, Santiago, Chile. Meets fourth Friday of each month.

Sociedad Colombiana de Radiologia
Secretary-General, Dr. Armando Uribe, Hospital Militar Central, Apartado aéreo No. 5804, Bogotá, Colombia. Meets last Thursday of each month.

Sociedad Ecuatoriana de Radiología y Fisioterapía
Secretary, Dr. Carlos Palau, Av. Bogotá 206, Guayaquil, Ecuador.

Sociedad Paraguaya de Radiología
Secretary, Dr. Miguel González Addone, 15 de Agosto 322, Asunción, Paraguay.

Sociedad Peruana de Radiologia
Secretary-General, Dra. Ladis Delpino, Instituto de Radiología "Cayetano Heredia" Hospital Arzobispo

Loayza, Lima, Perú. Meets monthly except during January, February and March.

Sociedad de Radiologica del Atlantico
Secretary, Dr. Raul Fernandez, Calle 40 #41–110, Baranquilla, Colombia. Society meets monthly at the Instituto de Radiología.

Sociedad de Radiología, Cancerología y Física Médica del Uruguay
Secretary-General, Dr. José Claussius, Av. Agraciada 1464, piso 13, Montevideo, Uruguay.

Sociedade de Radiología de Pernambuco
Secretary, Dr. Manoel Medeiros, Instituto de Radiologia da Faculdade de Medicina da Universidade do Recife, Caixa Postal 505, Pernambuco, Brazil.

Sociedad de Roentgenología y Medicina Nuclear de la Provincia de Córdoba
Secretary-General, Dr. Lucas C. Di Rienzo, Ave. Grl. Paz. 151, Córdoba, Argentina.

Sociedad Venezolana de Radiología
Secretary-General, Dr. Modesto Rivero Gonzáles, Apartado No. 9362 Candelaria, Caracas, Venezuela. Meets monthly, third Friday at Colegio Médico del Distrito Federal, Caracas.

Continental Europe

Österreichische Röntgen-Gesellschaft
President, Dr. Konrad Weiss, Mariannengasse 10, Vienna 9, Austria. Meets second Tuesday of each month in Allgemeine Poliklinik.

Société Royale Belge de Radiologie
General Secretary, Prof. Simon Masy, Louvain, Belgium. Meets in February, March, May, June, September, October, November and December.

Société Européenne de Radiologie Pédiatrique
Permanent Secretary, Dr. Jaques Sauvegrain, Hôpital des Enfants-Malades, 149, rue de Sèvres, Paris 15e, France. *General Secretary*, Dr. H. Ludin, Department of Roentgenology, Basler Kinderspital, Basel, Switzerland. Annual meeting: Warsaw, Poland, May 22–24, 1969. *Secretary*, Dr. Kasawery Rowinski, Zaklad Radiologii Pediatrycynej Akademii Medycznej, Marzalkowska 24, Warszawa, Poland.

Société Française d'Electroradiologie Médicale, and its branches: Société du Sud-Ouest, du Littoral Méditerranéen, du Centre et du Lyonnais, du Nord, de l'Ouest, de l'Est, et d'Alger et d'Afrique du Nord. Central Society meets third Monday of each month, except during July, August and September, rue de Seine 12, Paris, France.
Secretary-General, Dr. Ch. Proux, 9 rue Daru Paris 8e, France.

Československá Společnost pro Roentgenologii a Radiologii
Secretary, Dr. Robert Poch, Praha 12, Srobárova 50, Czechoslovakia. Meets monthly except during July, August and September. Annual general meeting.

Deutsche Röntgengesellschaft
President, Professor Dr. med. Hanno Poppe, Radiologische Univ.-Klinik, Gossler Str. 10, 34 Göttingen, Germany.

Società Italiana di Radiologia Medica e di Medicina Nucleare
Secretary, Dr. Ettore Conte, Ospedale Mauriziano Torino, Italy. Meets annually.

Nederlandse Vereniging voor Radiologie
Secretary, Dr. C. B. A. J. Puijlaert, Prof. Dondersstraat 73, Tilburg, Netherlands.

Scandinavian Radiological Society
Secretary-General, Professor C. E. Unnérus, M.D., Hagalung-Tapiola, Havsvindsvägen 5 C., Finland. Next meeting: Finland, Helsinski, June 11–14, 1969. This is the Fiftieth Anniversary Congress of the members of the 5 Scandinavian Radiological Societies, held in scandinavian languages.

Sociedad Española de Radiología y Electrología Médicas y de Medicina Nuclear
Secretary, Juan Gómez López, Villanueva, 11, Madrid 1. Meets every second Friday of each month, Oct. to June, inclusive, in Madrid.

Schweizerische Gesellschaft für Radiologie und Nuklearmedizin (Société Suisse de Radiologie et de Médecine Nucléaire)
Secretary, Dr. Max Hopf, Effingerstrasse 47, Bern, Switzerland.

Asia

Indian Radiological Association
Secretary, Dr. R. F. Sethna, Navsari Building, Hornby Road, Bombay 1, India.

Indonesian Radiological Society
Secretary, Professor Sjahriar Rasad, Taman Tjut Mutiah I Diakarta, Indonesia

Iranian Radiological Society
Secretary, Dr. Issa Yaghmai, P.O. Box No. 14-1151, Teheran, Iran. The Society meets on the second Saturday of each month.

Vol. 105, No. 3

ABSTRACTS OF RADIOLOGICAL LITERATURE

INDEX TO ABSTRACTS

ROENTGEN DIAGNOSIS

Head

Lorber, J., and Zachary, R. B.: Primary congenital hydrocephalus: long term results of controlled therapeutic trial 712
Ruvalcaba, R. H. A., Reichert, A., and Smith, D. W.: Smith-Lemli-Opitz syndrome: case report 712

Neck and Chest

Friedmann, G., and Tismer, R.: Candida oesophagitis 712
Campbell, D. R., Brown, B., St. J., and Manchester, J. S.: An evaluation of radiopacity of various ingested foreign bodies in pharynx and esophagus 713
Gregor, W. M., and Lucke, H. H.: Amyloidosis of bronchus resembling carcinoma 713
Darke, C. S., and Lewtas, N. A.: Selective bronchial arteriography in the demonstration of abnormal systemic circulation in the lung 714

Abdomen

Colwell, E. J. *et al.:* Jejunal morphological characteristics in South Vietnamese residents: a preliminary report 714
Leone, A. J., Jr., and Bryan, C. S.: Leiomyosarcoma of the small bowel demonstrated by selective superior mesenteric angiography ... 715
Soter, C. S.: The use of barium in the diagnosis of acute appendiceal disease: a new radiological sign 715
Thomford, N. R., Rybak, J. J., and Pace, W. G.: Toxic megacolon 715
Orme, R. L'E., and Eades, S. M.: Perforation of the bowel in the newborn as a complication of exchange transfusion 715
Corkery, J. J. *et al.:* Colonic perforation after exchange transfusion 716
McSherry, C. K., Stubenbord, W. T., and Glenn, F.: The significance of air in biliary system and liver 716
Stephens, P. J. T., and Hudson, P.: Spontaneous rupture of spleen in plasma cell leukemia 716

Genitourinary System

Rusiewicz, E., and Reilly, B. J.: The significance of isolated upper pole calyceal dilatation 717
Lubin, E., Levitus, Z., and Shimeoni, A.: Rapid sequential kidney scanning with ^{131}I-hippuran 717

Nervous System

Fox, J. E., Batsakis, J. G., and Owano, L. R.: Unusual manifestations of chordoma: report of two cases 717

Skeletal System

Nathan, F. F., and Bickel, W. H.: Spontaneous axial subluxation in child as first sign of juvenile rheumatoid arthritis 718
March, H. C.: Congenital pseudoarthrosis of the clavicle 718
Reid, M. McC., and Fannin, T. F.: Extensive vascular calcification in association with juvenile rheumatoid arthritis and amyloidosis 718
Lee, J. B. *et al.:* Familial pseudohypoparathyroidism: role of parathyroid hormone and thyrocalcitonin 718
Ooi, Y. *et al.:* Acquired spondylolysis in child and young adult: report of two cases 719
Weinstein, J. D., Dick, H. M., and Grantham, S. A.: Pseudogout, hyperparathyroidism, and carpal-tunnel syndrome: case report 719

Blood and Lymph System

Strickland, B.: An angiographic sign of persistent ductus arteriosus 720

ROENTGEN DIAGNOSIS

Head

Lorber, John and Zachary, R. B. Primary congenital hydrocephalus: long term results of controlled therapeutic trial. *Arch. Dis. Childhood*, Oct., 1968, *43*, 516–527. (From: The Department of Child Health, University of Sheffield, and Children's Hospital, Sheffield, England.)

The authors report 30 consecutive cases of primary congenital hydrocephalus.

The hydrocephalus, as far as could be ascertained, was due neither to intrauterine infections nor to postnatal cerebral trauma or infection. No associated spina bifida cystica or other complex multiple congenital deformities were present.

The degree of hydrocephalus was determined by ventriculography and classified: Grade I, very mild hydrocephalus; Grade II, cerebral mantle measuring between 15 and 35 mm.; and Grade III, cerebral mantle of less than 15 mm.

Following the diagnosis of hydrocephalus, the patients were allocated by random selection to one of two groups. One group was treated by operation just after the diagnosis was made and the other group acted as control with no operation performed until it became clear that conservative treatment had failed. The immediate operative treatment utilized was the technique of ventriculocaval shunt and the Holter valve. All but 2 of the control cases were later operated on because of the rapid progression of their condition and the development of neurologic and intellectual deterioration.

Five deaths occurred, at least 3 and possibly 4 being due to complications of operative procedures and in at least 8 others complications due to the "shunt" led to serious intellectual or neurologic deterioration in those who did well before blockage or infection of the shunt tube.

The authors state that despite the complications, the high survival figure of 83 per cent and the fact that 84 per cent of the survivors are of normal intellect show the advance made in this field of treatment by utilizing ventriculocaval shunting and the Holter valve. Half of the survivors have normal size heads and none have shown gross cranial enlargement.

The study indicates that large heads in hydrocephalic children are avoidable with early treatment. —*Lionel W. Young, M.D.*

Ruvalcaba, R. H. A., Reichert, Albert, and Smith, David W. Smith-Lemli-Opitz syndrome: case report. *Arch. Dis. Childhood*, Oct., 1968, *43*, 620–623. (From: Rainer School, Department of Institutions, Buckley, Washington, and the Department of Pediatrics, University of Washington, Seattle, Wash.)

The authors report a case of Smith-Lemli-Opitz syndrome showing 2 previously unreported features: (1) hypoglycemia after prolonged fasts and ketogenic diet; and (2) morphologic anomalies of brain.

The Smith-Lemli-Opitz syndrome was first described by Smith *et al.* in 1964 and has been characterized by: failure to thrive, mental retardation, severe vomiting in early life, growth retardation, microcephaly, broad tipped nose with anteversion of the nostrils, broad alveolar ridges of maxillae, ptosis of eyelids, asymmetric short fingers, and syndactyly of second and third toes as well as cryptorchidism, hypospadias, and/or chordee in the male.

This $5\frac{3}{4}$ year old boy reported had no abnormalities on excretory urography. A pneumoencephalogram showed "symmetric generalized dilatation of the lateral and 3rd ventricles and a smaller than usual cerebellum." Plain roentgenograms of the skull revealed moderate flattening of the occipital bone. Roentgenograms of the hands demonstrated fusion of the proximal and central parts of the 4th and 5th metacarpals in a "Y" shape with a rudimentary 5th metacarpal. The right thumb phalanges were hypoplastic while those of the feet showed subluxation of the distal phalanges of the 4th and 5th toes.

The authors indicate that it is not known if the 2 new features are usual components of the syndrome.—*Lionel W. Young, M.D.*

Neck and Chest

Friedmann, G., and Tismer, R. Candida oesophagitis. *German Med. Monthly*, Sept., 1968, *13*, 418–420. (From: The Department of Radiology, University of Köln, Köln, Germany.)

Primary Candida mycoses are rare and the result of exogenous infection. Secondary infection of the respiratory, genitourinary and gastrointestinal tracts usually occurs from primary infection of the skin or nasal cavities by fungi which are only potentially pathogenic. Lowering of body resistance because of debilitating disease (renal failure, progressive neoplastic metastases) or through therapeutic measures (steroids, antibiotics, cytotoxins) may allow the saprophyte to become pathogenic.

Laboratory demonstration of Candida from an organ or sputum is only presumptive, not confirmatory evidence of infection. Serum reactions are useful if there is fluctuation in titer with a maximum titer greater than 1:160. Proof of candidiasis consists of demonstrating organisms in tissues (*e.g.*, blood), or in secretions (*e.g.*, pleural effusions).

Secondary Candida infection usually involves the mouth, larynx and pharynx, the respiratory tree, and also the vagina. Involvement of the esophagus is rare. Characteristically esophagitis presents as a

rapidly worsening painful dysphagia, heartburn and retrosternal pressure. Candida esophagitis results from the downward spread of the organism from a pharyngitis or stomatitis; however, the clinical evidence of involvement in these areas may be entirely lacking.

The roentgenologic features include mucosal deformities of varying size, completely irregular in shape and extent, giving the esophagus a "toothed" appearance. The mycotic ulcers vary in size and shape, extending over the entire mucosa and appearing as multiple niches. If contrast material penetrates the pseudomembrane, the esophagus appears to possess a double contour. The mucosal pattern has a course honeycombed appearance.

In advanced cases the esophageal wall is infiltrated by organisms and loses its distensibility. Peristalsis is superficial and slow, but may be completely absent. The esophagus may resemble a rigid tube resulting in prolonged adherence of contrast medium to the wall.

The differential diagnosis should include other conditions such as: esophageal varices, malignant neoplasms, reflux esophagitis, corrosive injuries, and the mucous membrane involvement by tuberculosis, syphilis, and Hodgkin's disease—all of which the authors feel can be readily differentiated from Candida esophagitis on the basis of clinical and roentgenologic grounds.

The prognosis of Candida esophagitis depends largely on the course of the primary disease, but early diagnosis and treatment with antimycotic drugs do provide for a favorable outcome. If unrecognized or untreated, the course progresses rapidly to involve the entire gastrointestinal tract and in some instances produce a septicemia. Only if the infection has been severe and all layers of the esophagus involved does the wall remain rigid and stenosed.

With the increasing use of drugs which lower cellular resistance the authors predict an increase in the incidence of Candida esophagitis.

The authors report 4 cases of Candida esophagitis. —*Donald Traicoff, M.D.*

Campbell, D. R., Brown, B., St. J., and Manchester, J. S. An evaluation of radioopacity of various ingested foreign bodies in pharynx and esophagus. *J. Canad. A. Radiologists*, Dec., 1968, *19*, 183–186. (From: Victoria General Hospital and Dalhousie University, Halifax, Nova Scotia, Canada.)

Roentgenologic studies of the pharynx and esophagus, when an ingested foreign body is suspected, can be limited to plain film examination, or contrast media may be used. Contrast media may often obscure a foreign body and they may hinder the endoscopist in his examination and attempt to remove a foreign object.

In order to evaluate the probable success in identifying an ingested foreign body with plain film roentgenographic study alone, the authors collected a number of specimens of bones and shells from the hospital kitchen; these were studied roentgenographically in a water tank phantom and were then placed in plastic nasogastric tubes for *in vivo* study. Lack of volunteers to swallow the tubes curtailed the study to a degree, and a staff member in the department finally became the only subject employed. The foreign bodies used included the usual commonly ingested fragments from pork chop, chicken, haddock, herring, broiler, lamb chop, lobster, ham, cod, and halibut.

The study was a disappointment to the authors because of the lack of radiopacity of the various foreign bodies. It lead to the conclusion that: (1) anteroposterior roentgenograms of the cervical and thoracic esophagus are not of value in searching for commonly ingested food elements; (2) when fish bones are suspected, one gains little by repeated attempts to visualize the foreign body with plain film roentgenograms alone; and (3) when other than fish bone foreign bodies are suspected, plain film roentgenograms of the cervical esophagus and oblique roentgenograms of the thoracic esophagus are of value.—*Richard E. Kinzer, M.D.*

Gregor, W. M., and Lucke, H. H. Amyloidosis of bronchus resembling carcinoma. *Canad. M. A. J.*, Nov. 9, 1968, *99*, 912–914. (Address: Dr. W. M. Gregor, Niagara Peninsula Sanatorium Association, P.O. Box 158, St. Catharines, Ontario, Canada.)

Primary amyloid disease of the respiratory tract generally occurs in the form of single or multiple deposits resembling tumors. The lung is seldom involved. Solitary amyloid "tumors" of the bronchus are rare. Only 4 cases were reported. Two of the cases were diagnosed following pneumonectomy for suspected bronchial carcinoma. The other 2 were confirmed by bronchoscopic biopsy.

The authors describe a case of a 58 year old woman complaining of cough and chest pain. Roentgenogram of the chest revealed portal atelectasis of the right middle lobe. Bronchography showed narrowing of the middle lobe bronchus and also of the right lower lobe bronchus just distal to the middle lobe take-off. Bronchial carcinoma was suspected. Biopsy at bronchoscopy was done and the pathologist's examination revealed the material to be amyloid. This was confirmed with staining with PAS, congo red and crystal violet.

There is no cure for bronchial amyloidosis at the present time. Bronchoscopic curettage, electrocoagulation and irradiation have been beneficial. Also right upper lobectomy with sleeve resection of the right stem bronchus excising the mass and re-anastomosing the middle and lower lobes to the trachea

has successfully been performed.—*M. A. Cortese, M.D.*

Darke, Christopher S., and Lewtas, Norman A. Selective bronchial arteriography in the demonstration of abnormal systemic circulation in the lung. *Clin. Radiol.*, Oct., 1968, *19*, 357–367. (From: The Respiratory Function Unit and Department of Radiology, The Royal Infirmary, Sheffield, England.)

Enlargement of the bronchial arteries occurs in 2 main conditions: (1) when the pulmonary blood flow is diminished, such as in congenital heart disease, and (2) when inflammatory or neoplastic tissue replaces normal lung tissue. The authors' technique consists of selective bronchial arteriography following thoracic aortography. The latter procedure often identifies the location of enlarged bronchial artery orifices.

Venous drainage from bronchial arteries is divided somewhat unequally in that two-thirds of the flow goes to the pulmonary vein and one-third to the systemic circulation by the azygos system. In 50 per cent of the authors' patients with severe bronchiectasis, markedly dilated bronchial arteries supplied the affected area. Both the "forward flow" and the "reverse flow" was noted. The former is manifested by anastomosis with pulmonary capillaries and through pulmonary veins to the left side of the heart. The latter pattern of flow is centripetal up the pulmonary artery toward the heart. Similar findings have been noted in the absence of the left pulmonary artery seen in some cases of tetralogy of Fallot and in isolated unilateral absence of a pulmonary artery. This has also been noted to occur in major pulmonary artery embolus or thrombosis.

Studies of the hemodynamic effects of increased bronchial circulation suggest that the forward flow occurs when there is no significant increase of the vascular resistance, whereas the reverse type of flow occurs when the vascular resistance is increased, although not to systemic levels. This phenomenon may thus explain the appearance of occlusion of a lobar pulmonary artery demonstrated on pulmonary angiography.

The forward flow, in effect, creates a left to right shunt which will result in overload of the left ventricle and possibly hypertrophy. This series of events may well explain the left ventricle hypertrophy occasionally seen with cor pulmonale without other obvious causes for left ventricle hypertrophy. This has also been suggested as a cause of hemoptysis, since blood at systemic pressure is being shunted into thin-walled pulmonary vessels which subsequently rupture.

The same explanation may possibly be important in the associated hemoptysis and primary pulmonary malignancy as opposed to metastatic disease, since metastatic disease is generally felt to be supplied by the pulmonary artery and in primary tumors by the bronchial arteries. The 3 signs of malignant tumors of the lung noted in these and previous studies are: (1) dilated, tortuous bronchial arteries, (2) pathologic vessels, and (3) systemic pulmonary shunts. Unfortunately, some malignant tumors are avascular and some inflammatory lesions have increased vascularity.

In conclusion, the authors state that possibly the surgical relief of these anastomoses may be as important as relieving the primary disease in and of itself, in that: (1) the overload of the left ventricle is obviously decreased, and (2) recurrent hemoptysis may be more adequately controlled.—*Major James Stevenson, MC*

Abdomen

Colwell, Edward J., Welsh, Jack D., Legters, Llewellyn J., and Proctor, Robert F. Jejunal morphological characteristics in South Vietnamese residents: a preliminary report. *J.A.M.A.*, Dec. 2, 1968, *206*, 2273–2276. (From: Walter Reed Army Institute of Research, Walter Reed Army Medical Center, Washington, D.C. 20012.)

Inflammation of the small bowel is a morphologic manifestation of tropical sprue.

In the Republic of Vietnam (RVN), there are no data on the prevalence of tropical sprue in native or foreign residents; studies accomplished on a random sample of US Army personnel returning to the United States after deployment in RVN for 6 month periods showed a 6 per cent prevalence of jejunitis. Most of those with inflammatory changes in jejunal mucosa were engaged in military operations in the Mekong River delta.

The purpose of this investigation is to determine if similar jejunal morphologic alterations were present in native Vietnamese residing in the Mekong River delta.

The experimental subjects consisted of 16 Vietnamese patients undergoing laparotomy at Phong Dinh Province Hospital in the city of Can Tho. The ages ranged from 7 to 76 years. There were 10 females and 6 males. A traumatic abdominal wound was the indication for laparotomy in 9 patients. In the remaining 7, nontraumatic indications were present. At laparotomy, a biopsy specimen of the jejunum was obtained at a point 12 to 24 inches from the ligament of Treitz.

Jejunal mucosal specimens from 13 asymptomatic white North American volunteers, collected independently of specimens from Vietnamese, were used for comparison. None had resided in tropical areas. None had anemia, steatorrhea, or abnormal xylose absorption.

Five to seven villi in each specimen were measured. The average of the measurements was considered to

be representative of the section. Villus branching, fusion, knobbing, and variations in size and shape were graded as none, moderate, or marked.

Significant morphologic alterations were present in the jejunal mucosa of Vietnamese subjects when compared with that of North Americans. In the former, villus height was shorter and broader. Absolute crypt height was increased. Alterations in the histologic character of jejunal mucosa from Vietnamese subjects were also present when compared with jejunal mucosa from North Americans. Branching, fusion, and knobbing of villi were more frequent. Variations in villus size and shape were more pronounced. Eosinophilic cellular content was greater in tissue sections from Vietnamese.

Measured values for the two populations are shown in a scattergram. Differences between the arithmetic means for all mucosal dimensions in the two groups were statistically highly significant.

Neither trophozoites of *Giardia lamblia* nor larvae of hookworm or *Strongyloides stercoralis* were observed in tissue sections. Morphologic alterations did not appear to be related to age, sex, or the type of surgical lesion.

The morphologic changes in Vietnamese were similar to those reported from Thailand, Pakistan, Malaysia and Hong Kong.—*Stephen N. Tager, M.D.*

Leone, Anthony J., Jr., and Bryan, Charles S. Leiomyosarcoma of the small bowel demonstrated by selective superior mesenteric angiography. *J. Canad. A. Radiologists*, Sept., 1968, *19*, 126–129. (From: The Departments of Radiology and Pathology, The Johns Hopkins Medical Institutions, Baltimore, Md.)

The authors report a case of jejunal low-grade leiomyosarcoma which presented with the history of recurrent moderate massive bleeding.

The diagnosis was made with superior mesenteric arteriography which showed large arterial feeders, irregular tumor vessels, and early dense filling of draining veins. The angiographic findings were similar to those of reported benign leiomyomas.—*Gonzalo Chua, M.D.*

Soter, Constantine S. The use of barium in the diagnosis of acute appendiceal disease: a new radiological sign. *Clin. Radiol.*, Oct., 1968, *19*, 410–415. (From: The Department of Radiology and Nuclear Medicine, Northwest Community Hospital, Arlington Heights, Ill.)

When clinical manifestations of acute appendicitis are obscure, a barium enema done without preparation may be helpful in clarifying the diagnosis.

Five kinds of information may be obtained: (a) Position of the cecum and appendix, *i.e.*, whether or not the appendix is retrocecal; (b) demonstration of a completely patent appendiceal lumen excludes appendicitis; (c) irregularity of the appendiceal lumen with kinks, and especially cut-offs are usually associated with appendiceal disease; (d) a pressure effect on the tip of the cecum, sometimes double, resembling a reverse 3 indicates appendicitis; (e) slight extrinsic pressure on, or spasm and irritability of, the terminal ileum may be seen.

Forty cases of suspected appendicitis were examined and 6 of the cases are reported and illustrated.—*Harvey I. Meyers, M.D.*

Thomford, Neil R., Rybak, James J., and Pace, William G. Toxic megacolon. *Surg., Gynec. & Obst.*, Jan., 1969, *128*, 21–26. (From: The Department of Surgery, The Ohio State University College of Medicine, Columbus, Ohio.)

The Ohio State University Hospitals admitted 623 patients with a diagnosis of ulcerative colitis from January 1, 1953 through December 31, 1967. Of these, 23 or 3.7 per cent had an episode of toxic megacolon. This is described as an acute fulminating event in ulcerative colitis in which there is rapid dilatation of the colon. All 23 patients had anorexia, abdominal cramps, and diarrhea. All were acutely ill, and all had generalized tenderness of the abdomen. However, the physical findings of abdominal distention were mild or absent in 8 of the patients at the time dilatation of the colon was established roentgenographically.

Nineteen patients underwent an operative procedure and 16 of these had one or more postoperative complications with 5 or 26.3 per cent dying during the early postoperative period.

Four patients were managed medically and 1 died from perforation of the cecum, possibly initiated by barium enema-induced dilatation of the colon.

The authors state that "dilatation of the colon during episodes of fulminating ulcerative colitis appears related to marked peritoneal and subserosal inflammation, severe destruction of the muscle layers of the wall, and damage to the myenteric plexus."

Medical management of these patients will fail in many instances and surgical procedures are necessary.—*Richard E. Kinzer, M.D.*

Orme, R. L'E., and Eades, Sheila M. Perforation of the bowel in the newborn as a complication of exchange transfusion. *Brit. M. J.*, Nov. 9, 1968, *2*, 349–351. (From: Dr. R. L.'E. Orme, Senior Registrar in Paediatrics, Devon and Exeter Clinical Area, Devon, England.)

Six newborns who received exchange transfusions for Rh incompatibility and another who received prolonged intravenous fluid therapy via an umbilical

vein catheter developed spontaneous perforations of the small or large bowel.

The roentgenologic findings are described in 5 of the patients. Pneumoperitoneum was seen in 1, intestinal dilatation in several, and an ileocolic fistula was demonstrated by barium enema in another. Four patients survived.

The pathologic findings resembled necrotizing enterocolitis. The etiology is thought to be related to local vasomotor disturbances, or systemic hypotension, exacerbated by hypoxia or shunting of blood in the bowel wall bypassing the mucosa.—*Harvey I. Meyers, M.D.*

Corkery, J. J., Dubowitz, V., Lister, James, and Moosa, A. Colonic perforation after exchange transfusion. *Brit. M. J.*, Nov. 9, 1968, *2*, 345–349. (From: Dr. J. J. Corkery, Senior Surgical Registrar, Paediatric Surgical Unit, the Children's Hospital, Sheffield, England.)

Four infants are reported who survived colonic perforation following exchange transfusion. All were treated surgically.

Roentgenographically, 2 of the patients showed pneumoperitoneum, and 2 showed intestinal distention, 1 with increased intraperitoneal fluid. A follow-up barium enema showed narrowing at the previous site of perforation.

It is believed that the perforations are caused by some type of vascular lesion, although the authors' explanation as to how this may occur by pooling of the exchange transfusion in the portal system is difficult to connect with the pathologic changes noted.—*Harvey I. Meyers, M.D.*

McSherry, Charles K., Stubenbord, William T., and Glenn, Frank. The significance of air in biliary system and liver. *Surg., Gynec. & Obst.*, Jan., 1969, *128*, 49–61. (From: The Department of Surgery, The New York Hospital–Cornell Medical Center, New York, N. Y.)

Contrast is the basis for roentgenographic penetration and interpretation. Air in the stomach was described as a contrast medium as early as 1899. Air or gas shadows in an abnormal position are almost always a sign of serious disease or injury. Air in the gallbladder usually signifies infection but may be due to fistula of intestinal tract. Air in the bile ducts may have the same significance and air in the liver is usually due to infection with abscess.

Eleven case histories of patients presenting with air in the liver or biliary ductal systems are reported. Each is well illustrated with roentgenographic reproductions and excellent line drawings. The reproductions of the roentgenograms are superb.

The pathologic processes illustrated range from a very rare emphysematous cholecystitis to an even more uncommon biliary bronchial fistula.

This is recommended reading for radiologists and surgeons.—*Richard E. Kinzer, M.D.*

Stephens, P. J. T., and Hudson, Page. Spontaneous rupture of spleen in plasma cell leukemia. *Canad. M. A. J.*, Jan. 4, 1969, *100*, 31–34. (Address: P. J. T. Stephens, M.D., Department of Pathology, Victoria Hospital, London, Ontario, Canada.)

A case is reported of an indisputable plasma cell leukemia presenting with anemia and plasmacytosis in a middle aged Negro woman. Remission was obtained with melphalan and prednisone lasting a year, then recurrence with anemia, impending renal failure, thrombocytopenia, and hemorrhage into the peritoneal cavity with splenic rupture, developed. Laparotomy was followed by postoperative deterioration of her condition and death, with subarachnoid hemorrhage and widespread plasma cell infiltration of the viscera, particularly of the spleen and its capsule.

Splenic rupture in the presence of enlargement from any cause has been known for centuries, especially when trauma is involved; many etiologic possibilities for spleen enlargement are listed. Some of the similarities and differences between multiple myeloma and plasma cell leukemia are discussed, and the interesting fact that an hemorrhagic diathesis is more common in plasma cell leukemia is emphasized.

Because rupture of the spleen is often lethal, diagnosis prior to rupture is imperative, as splenectomy can often be safely carried out. One should be particularly wary in the patient with splenic infarction, diagnosable by clinical examination, roentgenography and scintiscanning in a patient with an hemorrhagic diathesis.

The pathogenesis of splenic rupture rests on 2 possibilities: either the capsule is damaged, as by infiltration, infection, or infarction; or the normal capsule is stretched beyond tolerance by rapidly expanding splenic contents subject to malignant infiltration, hemorrhage or infection.

The 3 factors prominent in leukemic spleen rupture are infarction, leukemic infiltration and coagulation defect. Several causes of infarction are discussed which in addition to capsular invasion by leukemic cells can be found with lymphatic distention to the point of rupture. Capsular fibroblasts may also be directly affected and die or lose their normal cohesion.

The authors suggest that splenic rupture may be seen with increasing frequency as the life expectancy of the leukemia patient increases.—*Robert P. Andrews, M.D.*

Genitourinary System

Rusiewicz, E., and Reilly, B. J. The significance of isolated upper pole calyceal dilatation. *J. Canad. A. Radiologists*, Dec., 1968, *19*, 179–182. (Address: Dr. B. J. Reilly, Department of Radiology, The Hospital for Sick Children, Toronto, Ontario, Canada.)

Because of recent data suggesting that vascular impressions on the upper pole renal calyces may be associated with nephralgia or pyelonephritis, 2,000 pediatric intravenous pyelograms taken in the erect position were reviewed. Of these, only 55 demonstrated unipolar calyceal dilatation thought to be due to a partially obstructing vessel. No arteriograms were obtained, as in only 1 case was there a definite calyceal obstruction which seemed to warrent further investigation angiographically and surgically.

In this series the positive findings were almost equally distributed in the males and females but showed a marked preponderance for the right side (45 out of 55, or 81 per cent). Approximately half the patients had pain which could not be consistently characterized but none had costovertebral angle tenderness on the abnormal side. Half of the patients had clinical disease in the genitourinary tract but none had evidence of cortical destruction around the dilated calyx.

Follow-up intravenous pyelograms were obtained in one-third of the cases, although none had pain at the time of the repeat examination. The pyelographic appearance was unchanged in all but 1 case which exhibited decreased dilatation, so that angiography was not carried out in any of the patients.

The authors conclude that the abdominal pain, which might be nephralgia, is due to calyceal dilatation from partial vascular obstruction in only a small percentage of the cases, and that renal angiography is indicated only in the rare instance when localized pain and tenderness with renal cortical atrophy suggest that the symptoms result from this roentgenographic finding.—*Robert P. Andrews, M.D.*

Lubin, E., Levitus, Z., and Shimeoni, A. Rapid sequential kidney scanning with ^{131}I-hippuran. *N. M. J. Nuclear Med.*, Nov., 1968, *9*, 567–570. (From: Beilinson Hospital Medical School, University of Tel Aviv, Petah Tikva, Israel.)

Rapid sequential scans following the injection of I^{131}-hippuran were obtained using a conventional scanner. This made it possible to visualize the dynamics of the concentration and excretion of this material by the kidneys.

The information gained bv these sequential scans was especially useful in:

1. The interpretation of the causes of anemia in transplanted kidneys;
2. the early recognition of intra-abdominal urinary fistula; and
3. the recognition of localized ischemia of the kidneys.—*Isaac C. Reese, M.S.*

Nervous System

Fox, James E., Batsakis, John G., and Owano, Luis R. Unusual manifestations of chordoma: report of two cases. *J. Bone & Joint Surg.*, Dec., 1968, *50A*, 1618–1628. (Address: Dr. James E. Fox, 1335 East Catherine Street, Ann Arbor, Mich. 48104.)

Chordomas are usually non-metastatic neoplasms which arise from ectopic chordal foci found in the cranial, vertebral, and sacrococcygeal regions. These tumors are often indolent but progressive and the histopathology does not accurately portend their activity.

Two cases are reported. The first is that of a 58 year old woman who was found to have a large presacral chordoma which recurred several times over 6 years. She was admitted late in the course of her disease with multiple nodular pulmonary metastases. Death several months later, following transfusions and supportive care, ensued. Autopsy revealed extensive spinal, lymphatic, pulmonary, thoracic, and solitary cerebral spread by typical chordoma tissue.

The second case was that of a painful thoracic spine chordoma in a 67 year old woman who received 4,200 rads of cobalt 60 teletherapy, followed by only a few months improvement in her symptoms. Pain recurred and persisted, until $3\frac{1}{2}$ years later death due to pneumonia occurred following laminectomy for cord compression by the growing tumor. Histologically, the tumor was sarcomatous in its posterior portion and in its anterior portion it was similar to the original tumor. Several roentgenographic reproductions and photomicrographs are included.

Although chordomas often remain localized, there are varying reports in the literature indicating that 10 to 48 per cent may give rise to distant metastases. Only 10 cases of widespread metastases, as in the first case, could be found by authors. This is apparently more common following long clinical duration, repeated recurrences, and possibly following radiation therapy.

Treatment selection is difficult but combined surgical and radiotherapeutic techniques may be the best management. High dose radiation therapy over 5,000 rads seems to offer the best results but in view of the sarcomatous findings in the second case the possibility of radiation induced transformation must be considered.

The authors conclude that, although sarcomatous elements are reportedly found in chordoma, no previous reports of sarcomatous degeneration following radiation therapy for chordoma have been published. —*Robert P. Andrews, M.D.*

SKELETAL SYSTEM

NATHAN, FRED F., and BICKEL, WILLIAM H. Spontaneous axial subluxation in child as first sign of juvenile rheumatoid arthritis. *J. Bone & Joint Surg.*, Dec., 1968, *50A*, 1675–1678. (From: Section of Orthopedic Surgery, Mayo Clinic Foundation, Rochester, Minn. 55901.)

This is a report on a child admitted to the Mayo Clinic with spontaneous atlanto-axial subluxation and an elevated sedimentation rate. Lateral roentgenograms of the neck showed a 9 mm. space between the dens and the arch of the atlas.

Because of spinal cord compression the subluxation was reduced and maintained with wires and a bone graft used to promote fusion. Seven days after the operation the right knee became inflammed. Aspiration and synovial biopsy revealed subacute and chronic rheumatoid arthritis. The test for rheumatoid factor was weakly positive in the synovial fluid. It had been negative in blood tests prior to operation.

While the cervical spine is frequently involved during the course of juvenile rheumatoid arthritis and spondylitis, the authors could find only one other case in the literature in which subluxation at the atlanto-axial joint was the presenting finding. —*Everett H. Johnston, M.D.*

MARCH, H. C. Congenital pseudoarthrosis of the clavicle. *J. Canad. A. Radiologists*, Sept., 1968, *19*, 167–169. (Address: 7222 Castor Avenue, Philadelphia, Pa.)

Twenty-nine of the 30 reported cases of congenital pseudoarthrosis of the clavicle involved the right clavicle.

The hiatus occurs just lateral to the mid portion of the clavicle and results from failure in development of the precartilaginous bridge between the 2 clavicular centers.

The findings include acute angulation with shoulder sag. The ends are smooth and blunt in contrast to the tapering of pseudoarthrosis of the tibia which is associated with neurofibromatosis.

Birth fracture and cleidocranial dysostosis must be considered in the differential diagnosis.

The condition is mainly a cosmetic problem.

Some cases have been treated successfully with bone graft and internal fixation.—*J. T. Telle, M.D.*

REID, M. McC., and FANNIN, T. F. Extensive vascular calcification in association with juvenile rheumatoid arthritis and amyloidosis. *Arch. Dis. Childhood*, Oct., 1968, *43*, 607–610. (From: The Royal Belfast Hospital for Sick Children, and the Nuffield Department of Child Health and the Department of Pathology, The Queen's University of Belfast, Belfast, N. Ireland.)

The authors present the clinical and pathologic findings of a case of juvenile arthritis in a boy which began at age 2½ years and was complicated by amyloid disease at age 8¼ years with death at age 8½ years.

They emphasize the finding of vascular calcification found by a microscopic examination following necropsy of subendocardial tissues, of aorta, coronary, mesenteric, celiac, thyroid, hepatic, splenic, renal and intramuscular arteries. Postmortem roentgenography of the kidneys demonstrated vascular calcification particularly in the right kidney. Aside from some osteoporosis in the wrists there were no significant findings on roentgenograms obtained during life of calcification grossly demonstrable in any of the organ or vascular shadows.

The authors indicate that arterial calcification in childhood, although uncommon, has been described by many investigators in a variety of disorders such as syphilis, idiopathic hypercalcemia and hypervitaminosis D. Quite frequently in these conditions arterial calcification can involve the coronary arteries and death can occur in the first 6 months of life.—*Lionel W. Young, M.D.*

LEE, JAMES B., TASHJIAN, ARMEN H., JR., STREETO, JAMES M., and FRANTZ, ANDREW G. Familial pseudohypoparathyroidism: role of parathyroid hormone and thyrocalcitonin. *New England J. Med.*, Nov. 28, 1968, *279*, 1179–1184. (From: Saint Louis University School of Medicine, 1325 South Grand Boulevard, Saint Louis, Mo. 63104.)

In 1942 Albright and his colleagues described a clinical syndrome characterized by a short stature, abnormalities of bone, mental retardation, tetany, hypocalcemia, hyperphosphatemia and no phosphaturic response to exogenously administered parathyroid hormone. Albright termed this disorder pseudohypoparathyroidism.

Recently, thyrocalcitonin, a hypocalcemic polypeptide secreted by the mammalian thyroid gland, has been found in high concentration in the thyroid glands of patients with pseudohypoparathyroidism and has been considered to be of possible etiologic importance in the syndrome.

The authors describe a kindred in which 2 successive generations involving 3 family members were affected with the fully expressed syndrome of pseudohypoparathyroidism. In addition, special studies were carried out to examine the roles of the thyroid

and parathyroid glands in this disorder.

The family described consists of a 4 year old girl, a 6 year old boy, and a 28 year old mother.

A parathyroid biopsy and subtotal thyroidectomy were undertaken on the mother after the following points were considered: the possible etiologic roles of thyrocalcitonin and abnormalities of the parathyroid glands in pseudohypoparathyroidism; the persistence and severity of the symptoms ascribable to hypocalcemia; and the presence of pre-existing hypothyroidism, which had already established the need for thyroid replacement therapy. A left inferior parathyroidectomy and a bilateral subtotal thyroidectomy were performed for the purpose of assay of parathyroid hormone and thyrocalcitonin, respectively. The removed parathyroid gland was normal histologically. The thyroid gland showed many large follicles with abundant colloid and low, flat, inactive-appearing epithelium.

The parathyroid hormone was measured in peripheral venous plasma by radioimmunoassay with the use of a new antiserum of somewhat greater sensitivity than the one originally described. The results of immunoassays, show that all 3 patients with pseudohypoparathyroidism have at least normal, and probably elevated, levels of parathyroid hormone in their peripheral plasma. Thus, pseudohypoparathyroidism cannot be due to an absolute lack of parathyroid-hormone biosynthesis or release or to the synthesis of a biologically inert form of the hormone. Excised thyroid tissue of the mother was taken at surgery and was extracted and assayed biologically for thyrocalcitonin. These results indicate an increase of 50 to 100 times in the concentration of thyrocalcitonin in the thyroid gland.

The family reported in this study represents the second example of familial pseudohypoparathyroidism known to the authors in which the fully expressed syndrome was present in 2 successive generations. The mode of genetic transmission has been postulated to be either through autosomal or sex-linked dominant gene. Since male-to-male transmission is reportedly rare, sex-linked inheritance appears to be a more likely possibility. Transmission in the present family supports the hypothesis that the abnormal gene is carried on the X chromosome since the classic disorder was present in both the male and the female offspring of the affected mother.

The coexistence of hypothyroidism and pseudohypoparathyroidism has previously been noted, but has not been emphasized in the literature.

Significance of the association of hypothyroidism with pseudohypoparathyroidism is unknown. In some cases, isolated thyrotropin (TSH) deficiency may be an important factor.

Possible theoretic explanations for the hypocalcemia in pseudohypoparathyroidism are speculated upon in detail. Excessive secretion of thyrocalcitonin has also been considered as possibly implicated in the hypocalcemia.

For example, complete ablation of the thyroid gland should remove the source of thyrocalcitonin in man and thus ameliorate the hypocalcemia if it were caused by thyrocalcitonin excess. *However, thyroid ablation in the mother resulted in no change in the serum calcium.* Lastly, experimental evidence exists that chronic hypocalcemia results in a secondary increase in thyrocalcitonin in the rat thyroid gland.

Demonstration of abundant circulating parathyroid hormone in these patients and the inability to implicate thyrocalcitonin in the etiology of the hypocalcemia suggest that Albright's hypothesis of end-organ refractoriness to parathyroid hormone remains the best possibility as the fundamental defect in pseudohypoparathyroidism.—*Stephen N. Tager, M.D.*

Ooi, Yoshio, Suzuki, Yajuro, Sugawara, Sachiko, Yamazaki, Norio, and Morisaki, Naoki. Acquired spondylolysis in child and young adult: report of two cases. *J. Bone & Joint Surg.*, Dec., 1968, *50A*, 1649–1656. (From: Institute of Rehabilitation Medicine, New York University Medical Center, 400 East 34th Street, New York, N. Y. 10016.)

The first case is that of a child who had her first episode of low back pain at the age of 9 years. Over the next 4 years several more episodes occurred. Roentgenograms on the first occasion were normal but subsequently spondylolysis was demonstrated and gradually slight spondylolisthesis. Anterior fusion was carried out approximately 4 years after the onset of symptoms.

The second case is that of a 20 year old male laborer with a history of recurrent low back pain since the age of 15 years. Roentgenograms taken on two occasions prior to diagnosis of spondylolysis showed intact pedicles.

Neither patient was able to give a history of trauma.

There is a brief review of the literature. The authors use these cases to support the theory of developmental etiology: the result of both a predisposition (dysplasia) and stress on the pars interarticularis (erect stance and lumbar lordosis characteristic of man).—*Everett H. Johnston, M.D.*

Weinstein, Joel D., Dick, Harold M., and Grantham, S. Ashby. Pseudogout, hyperparathyroidism, and carpal-tunnel syndrome: case report. *J. Bone & Joint Surg.*, Dec., 1968, *50A*, 1669–1674. (From: The New York Orthopaedic Hospital, Columbia-Presbyterian Medical Center, New York, N. Y.)

The authors state that the carpal tunnel syndrome has been reported as associated with a variety of systemic diseases but it has not been described as

caused by pseudogout. Calcium pyrophosphate dihydrate crystals were found in the floor of the carpal tunnel and concretions of gritty material were adherent to tendon sheaths and the epineurium of the median nerve.

Clinically there was complete physiologic disruption of the median nerve bilaterally which operation did not relieve. Roentgenograms revealed soft tissue calcifications at both wrists, within all knee menisci, in the left patellar tendon, in the left elbow capsule and the articular cartilage of the femoral condyles.

Hyperparathyroidism was also present with consistently abnormal calcium and phosphorus levels. Uric acid levels were 7.7 mg. per cent twice and 8.8 mg. per cent once.

Removal of the parathyroid adenoma resulted in return of calcium and phosphorus levels to normal, but roentgenograms 4 months later showed no regression of the soft tissue calcifications.—*Everett H. Johnston, M.D.*

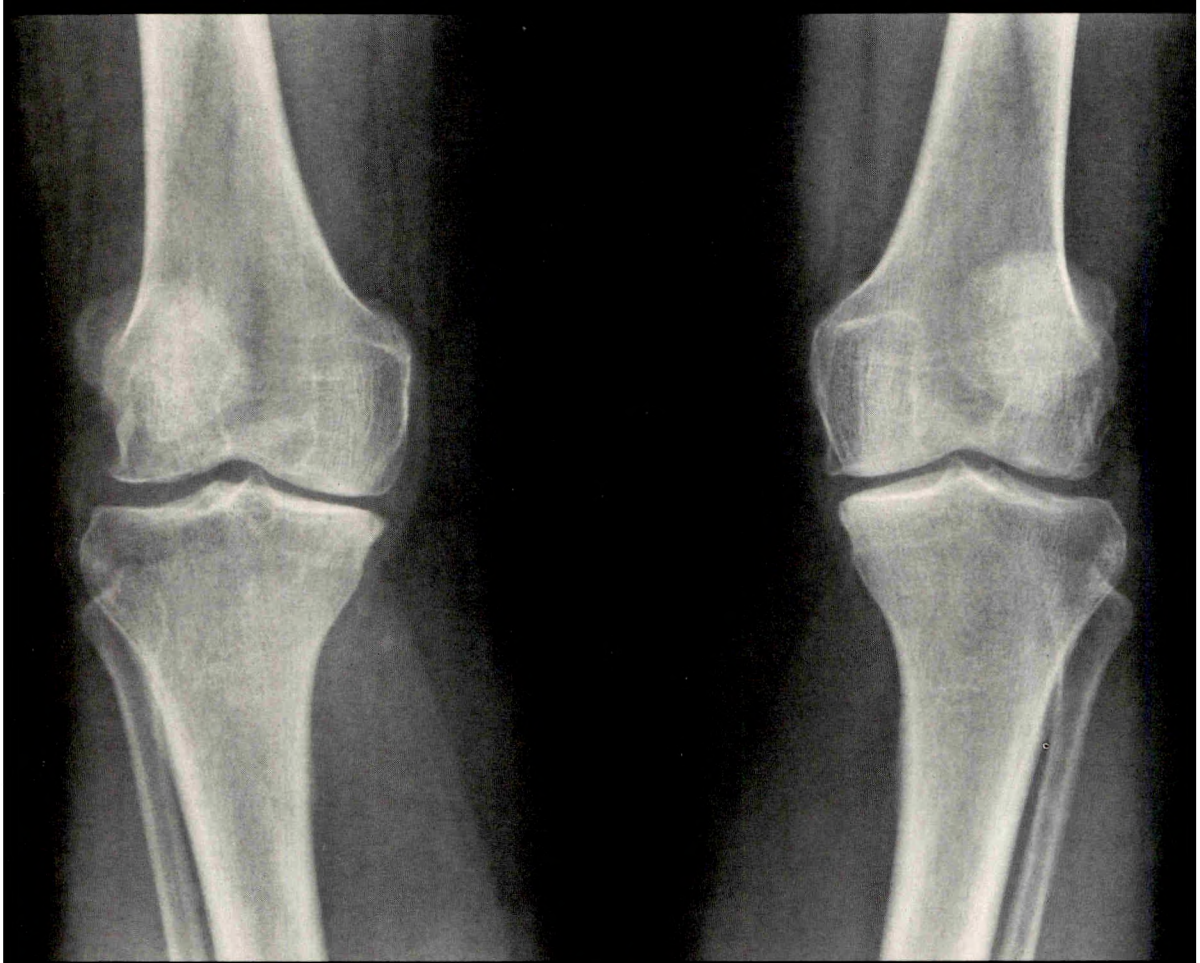
Blood and Lymph System

Strickland, Basil. An angiographic sign of persistent ductus arteriosus. *Clin. Radiol.*, Oct., 1968, *19*, 457–458. (From: The Westminster and Brompton Hospitals, London, England.)

The author describes a new sign of persistant ductus arteriosus which he has observed. This consists of differential filling of the peripheral branches of the 2 pulmonary arteries in the anteroposterior projection. This differential filling is evidenced by delayed filling of the left lung as opposed to the right.

In and of itself the sign is of no marked value; however, in complicated circumstances such as the presence of a large ventricular septal defect, either isolated or in association with tetralogy of Fallot, it becomes of special significance when only serial studies are available for interpretation and cine studies have not been utilized.—*Major James Stevenson, MC*

90 second proof



KODAK *RP* X-OMAT Medical X-ray Film — new emulsion for sharp and clearly defined information. More on next page.



KODAK *RP* X-OMAT Films give more information, time after time.

Quality is the reason you get radiographs with more information when you use KODAK *RP* X-OMAT Films.

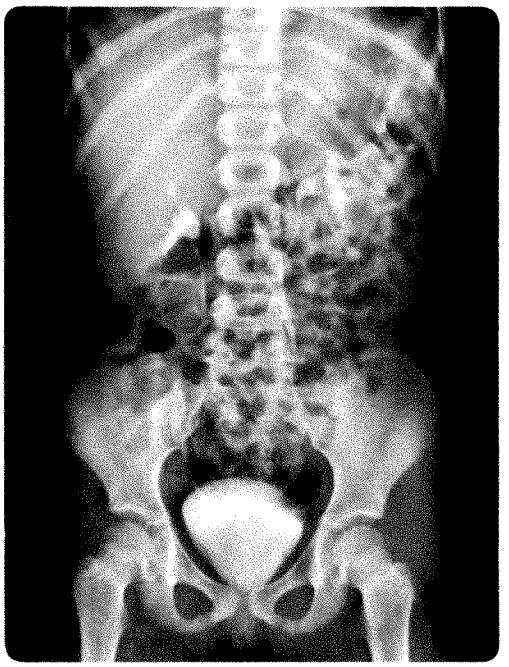
And film choice is an important part of Kodak quality. There are three films to choose from. The new, improved KODAK *RP* X-OMAT Film is the one represented here. It is especially effective in examinations where the subject contrast needs to be enhanced. Radiologists often say "it sparkles".

The two other films are KODAK *RP/L* and *RP/S* X-OMAT. No matter which of these films you choose to fulfill your requirements, the result will be more of the information you're after, time after time.

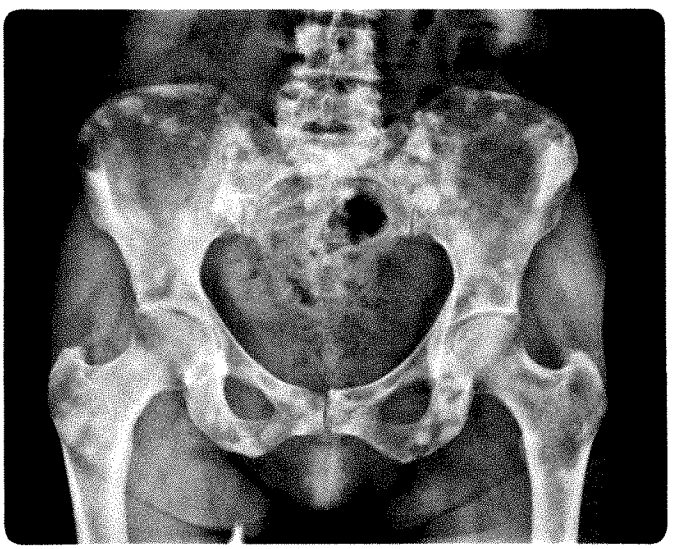
Quality processing is another part of the Kodak story. And it's a short one: 90 seconds from exposed film to reading with the KODAK *RP* X-OMAT Processor and the new system-balanced, low-temperature, long-life Kodak Chemicals.

For quality results in 90 seconds, select only the x-ray products that bear the name KODAK *RP* X-OMAT.

Kodak



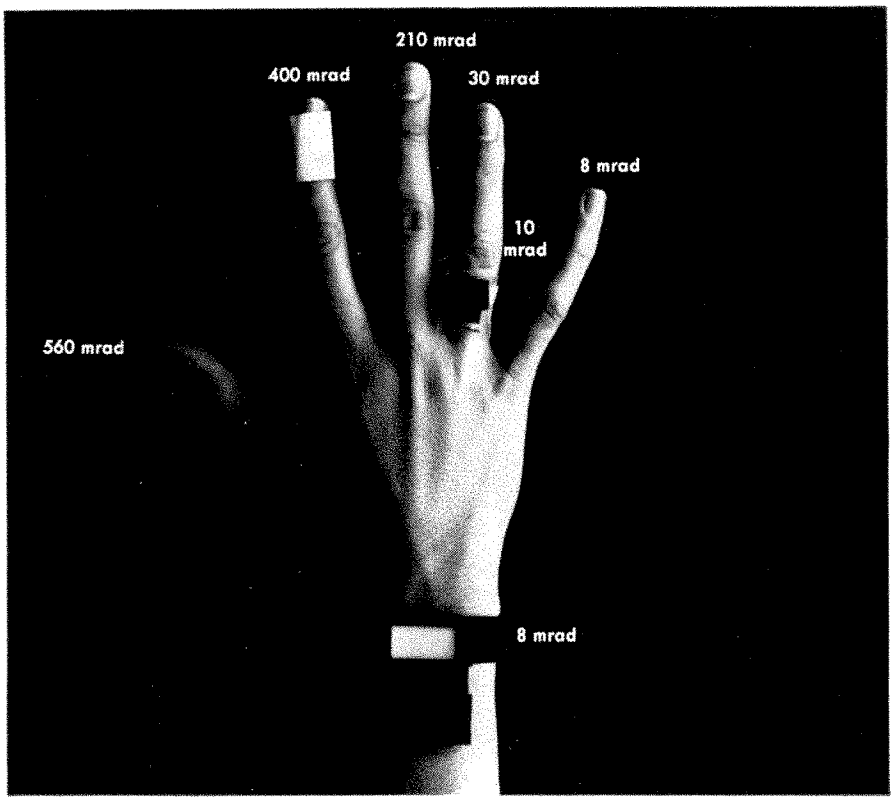
KODAK *RP* X-OMAT Medical X-ray Film — excellent detail and "sparkle" result from the new emulsion.



KODAK *RP* X-OMAT Medical X-ray Film — improved to enhance subject contrast.

EASTMAN KODAK COMPANY
Radiography Markets Division, Rochester, N.Y.

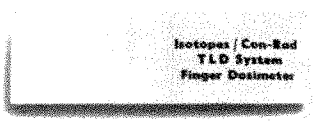
5 GOOD REASONS WHY YOU NEED FINGERTIP DOSIMETRY.



When you hold a 1 mg radium needle for as little as five minutes, your thumb receives a maximum dose as high as 560 mrad. A conventional photographic film dosimeter, wrist or ring, measures less than 2% of this dose. Only Isotopes LiF Teflon Finger Dosimeters can measure the dose at the points of maximum exposure — your fingertips.

What's more these rugged, thin, flexible and tissue equivalent Finger Dosimeters, with a dose range from 50 mr to 10^5 rads, measure the total dose from beta, gamma and x-rays to the sensitive layer of the skin.

Reasons enough, we think, to write or call ISOTOPES for full information. 50 Van Buren Avenue, Westwood, N.J. 07675 (201) 664-7070.

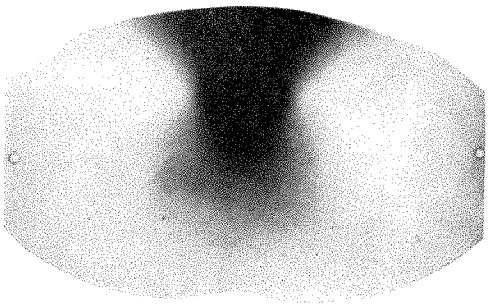


ISOTOPES
A TELEDYNE COMPANY

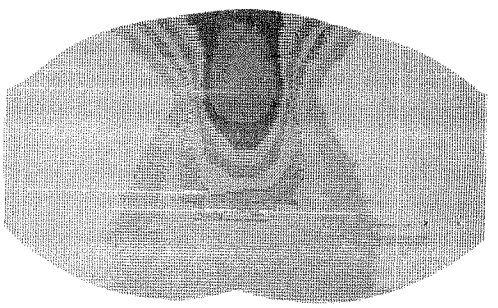
FILM ISODOSE CONTOUR PLOTTER

Model 3304

For rapid evaluation of dose distribution by film dosimetry.



Exposure pattern on developed film. This was exposed during an arc rotation treatment port on Cobalt 60.



Resultant isodose contour printout from film A. There are 168 symbols per sq. in.; plotted in 5% dose increments.

Minimize time constructing isodose curves from films containing dose distributions. Simulate and evaluate therapy with only short time on treatment machine. Evaluate beam shape, and test field homogeneity simply, fast and accurately. Make permanent records and quick checks on experimental therapy portals. Reduce film evaluation time from days to minutes.

FEATURING:

- All solid state integrated circuit design with modular construction for easy maintainability.
- Improved high speed 10 prints/seconds film reader and transport.
- High stability solid state densitometer with tracking, self aligning, single point light source.
- Reduced size, small compact table model; systems supplied as functionally complimenting instruments.
- Standard coded outputs and inputs, easy to interface with data handling equipment and accessories.

Use the same system for simple or multiple isotope scanning of brain, kidney, heart, and liver, etc., by adding up to two spectrometers. Three dimensional water tank — scanner for phantom studies will be available by mid 1969. For further information and reprints from "Radiology" and "Hospital Handbook" contact:

716 HANLEY
INDUSTRIAL COURT
ST. LOUIS, MO. 63144
PHONE (314) 644-2456

artronix
INSTRUMENTATION

IMPORTANT!

OBTAIN MAXIMUM MARKET PRICES... from the nation's largest buyer of used x-ray film...

donald McElroy inc.

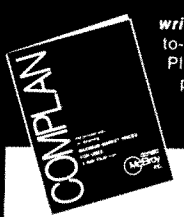
31 years of integrity

we purchase all brand and sizes of used x-ray film from anywhere in the United States . . . and we pay the freight cost.

we pay in advance if requested, or immediately upon the receipt and weight evaluation of your shipment.

our maximum market prices are gauged by the metals market and are adjusted continuously to reflect full value.

we offer 12-month, cumulative Incentive Payment Bonuses for consistent shipments of used x-ray film. You reduce storage problems, earn highest weight increment prices.



write for—your computerized, up-to-the-hour Quotation for Purchase Plan that assures you of our pledge to give . . . Maximum Market Prices.

DONALD McELROY INC.
3201 old glenview road
wilmette, illinois 60091

Please send me COMPLAN TODAY.

NAME _____

_____

_____

ADDRESS _____

CITY _____ STATE _____ ZIP _____



Du Pont focuses its science and energy on Diagnostic Clarity even at high KvP

Diagnostic Clarity need not suffer when you use high KvP technics. Not when you are using CRONEX® 4 x-ray film. CRONEX 4 has high contrast characteristics and an optically clear CRONAR® polyester base that give you radiographs with exceptional Diagnostic Clarity even at high KvP.

The advantages of high KvP radiography are many: reduced patient exposure, less chance of motion unsharpness, increased radiographic latitude, improved control of contrast, less heat in the x-ray tube. Now you can get them and Diagnostic Clarity, too . . . with CRONEX 4.

Your Du Pont Technical Representative can help you evaluate these advantages and is equipped with suggested high KvP technics for most anatomical views. Why not talk to him about it?

DU PONT **CRONEX X-ray Products**

Elementary Dr. Watson



Hunt helps you solve the great modern detective story.

Sherlock Holmes of Baker Street, the world's most famous detective, used the clues of romantic fiction to solve the mysteries of turn-of-the-century England. You, the diagnostic radiologist, interpret the patterns of a radiographic image and you solve the great modern detective story that diagnostic film reading is part of.

We, at Hunt, provide the chemistry, service and technical knowledge that helps you achieve consistent film development with the ultimate in sensitometric response. We have no vested interest in film. We're chemists with but one goal: **More information on any film through total processing control.**

HUNT PREMIUM 90/90 DEVELOPER AND REPLENISHER . . . the first ultra-concentrated chemistry for 90-second x-ray processing at the lowest temperature of any product offered to the profession. Premium 90/90 provides the highest contrast and density of any chemistry on the market.

HUNT ULTRA-MAT DEVELOPER AND REPLENISHER . . . the first ultra-concentrated, universal x-ray chemistry for normal temperature ranges accepted for all time cycles . . . 90-seconds, 3½ and 7 minutes. Ultra-Mat has been formulated to meet the speed and contrast levels inherent in the film of your choice with the lowest possible fog level.

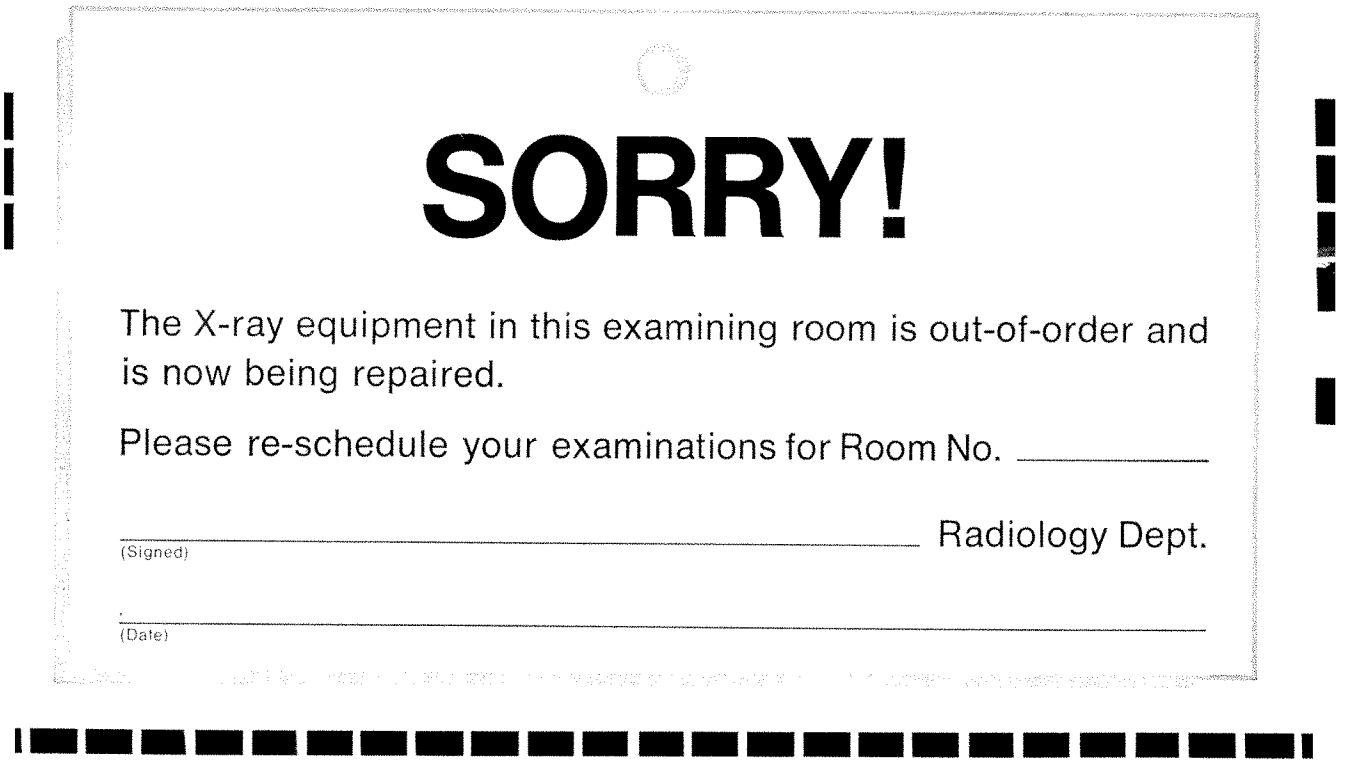
HUNT GRAPH-O-MAT® 90 FIXER-REPLENISHER . . . the recommended and tested fixer for automatic processing systems.

MANUFACTURING CHEMISTS • HUNT • ESTABLISHED 1905

PHILIP A. HUNT CHEMICAL CORPORATION

Palisades Park, New Jersey • Branches in Principal Cities • PHILIP A. HUNT COMPANY (CANADA) LTD. Toronto

Will your radiology department ever need one of these handy little signs?



Just our way of emphasizing some facts: Every minute that a vital piece of X-ray equipment is down is a lost minute—time that you never seem to be able to make up by re-scheduling examinations.

And when minutes stretch into hours and days of waiting for service, then your own difficulties in handling your work load are compounded by the inconvenience which your patients experience.

We of Standard X-ray have never been happy with these facts. We believe a tendency toward breakdowns is unacceptable in X-ray equipment. We've believed that for more than 50 years.

So we do things differently. We design X-ray equipment that makes downtime rare and day-in, day-out reliability an accepted fact.

How? For one thing, we make our equipment modular. Take our Ultima and our new Optima Series of X-ray Controls as examples. Every control is constructed of hand-crafted, modular components integrated to function as a single X-ray unit.

Which also means unparalleled reliability because each modular component is individually tested. So that the complete X-ray control will be one you can count on every time you press the "exposure" button. An X-ray unit that's easy to maintain—and easy to repair when the time *does* come.

Standard X-ray's brand of reliability doesn't stop at design, however. It includes the special care that goes into the manufacture of every unit. And the service available through your local Standard X-ray dealer. He's there not just because something may go wrong, but to see that everything is working right.

What we're saying, then, is that we can offer you what no one else can: a complete line of therapeutic and diagnostic X-ray equipment that you can rely on. Service you can rely on. And consultation and planning for the radiology department that puts reliability first.

See what we mean! Call your Standard X-ray dealer. (Write us for his name. Incidentally, would you like additional copies of our "Out-of-Order" sign? Ask about them when you write us.)

STANDARD

STANDARD X-RAY COMPANY
a division of Cenco Medical/Health
2600 S. Kostner Ave., Chicago, Ill. 60623

we wouldn't leave "well enough" alone!

improved Albumotope®—LS

Aggregated Radio-Iodinated (I^{131}) Albumin (Human) for Lung Scanning

introduced by Squibb...
improved by Squibb

■ Reduced Protein Content

Squibb has reduced the amount of protein by 50% while maintaining good lung scans.

■ Reduced Supernatant Activity

Squibb has sharply reduced the amount of radioactivity in the supernatant, decreasing the possibility of liver interference with the lung scan.

■ Reduced Unbound Iodine

Squibb has substantially reduced the amount of unbound iodine 131, effectively reducing the problem of blood background radioactivity.

Albumotope—LS—a good example of Squibb leadership in radiopharmaceutical research and development. Some people won't leave "well enough" alone.

Contraindications: Radiopharmaceuticals should not be administered to pregnant women or to persons under the age of 18 years unless the indications are very exceptional. Because iodide is excreted in human milk, aggregated radioalbumin should not be administered to nursing mothers.

Side Effects and Precautions: There have been no reported cardiovascular or other untoward effects attributable to Albumotope—LS. Extensive clinical use of Albumotope—LS has not borne out the hypothetical possibility that particles of large size might induce deleterious cardiovascular or cerebrovascular effects. The product appears to possess no antigenic properties. One patient with a known history of angioneurotic edema, who had been given Lugol's solution in conjunction with aggregated radioalbumin similar to Albumotope—LS, developed urticaria.

For full prescribing information, see package insert.

Available: As a sterile, nonpyrogenic, aqueous suspension. Each cc. contains approximately 0.5 mg. aggregated human serum albumin labeled with iodine 131. Not less than 90% of the aggregates are between 10 and 90 microns and none are more than 150 microns in size. The preparation also contains 0.9% (w/v) benzyl alcohol as a preservative. The potency ranges from 250 to 450 microcuries per cc. on date of assay

Medotopes®

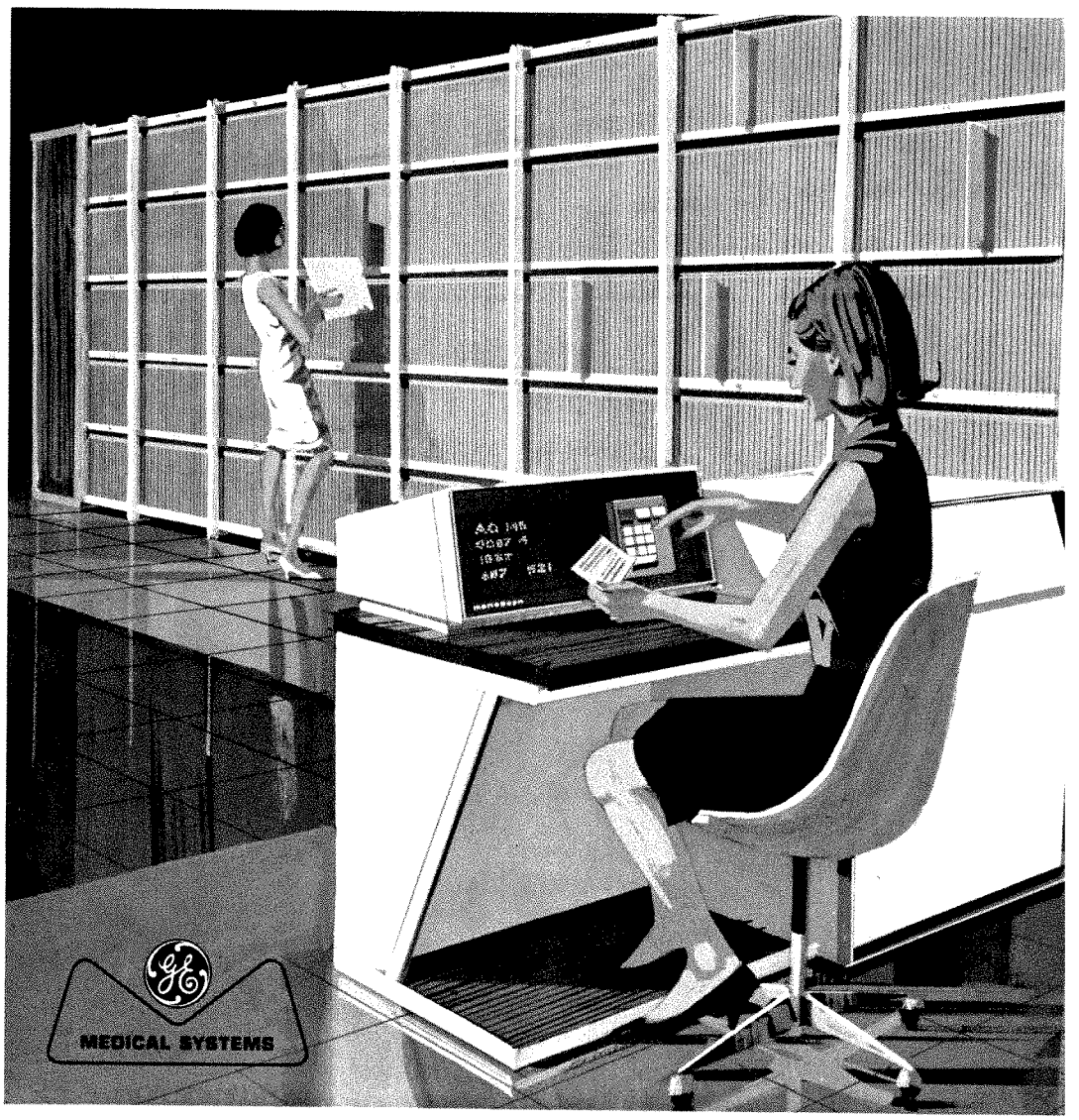
SQUIBB Division of Nuclear Medicine
East Brunswick, New Jersey 08816

the load lighteners

GE automated information

Films, films and more x-ray films
filing and "misfiling" problem. Ur
Two new GE information storage/
systems — Monoscan and Monot
lighten the load by replacing cost
consuming manual handling of fil
centralized storage and automatic

Monoscan, for "high activity" films,
absolute random placement in stora
folder, coded according to its infe
content, is produced immediately



id retrieval systems end outdated film/records handling

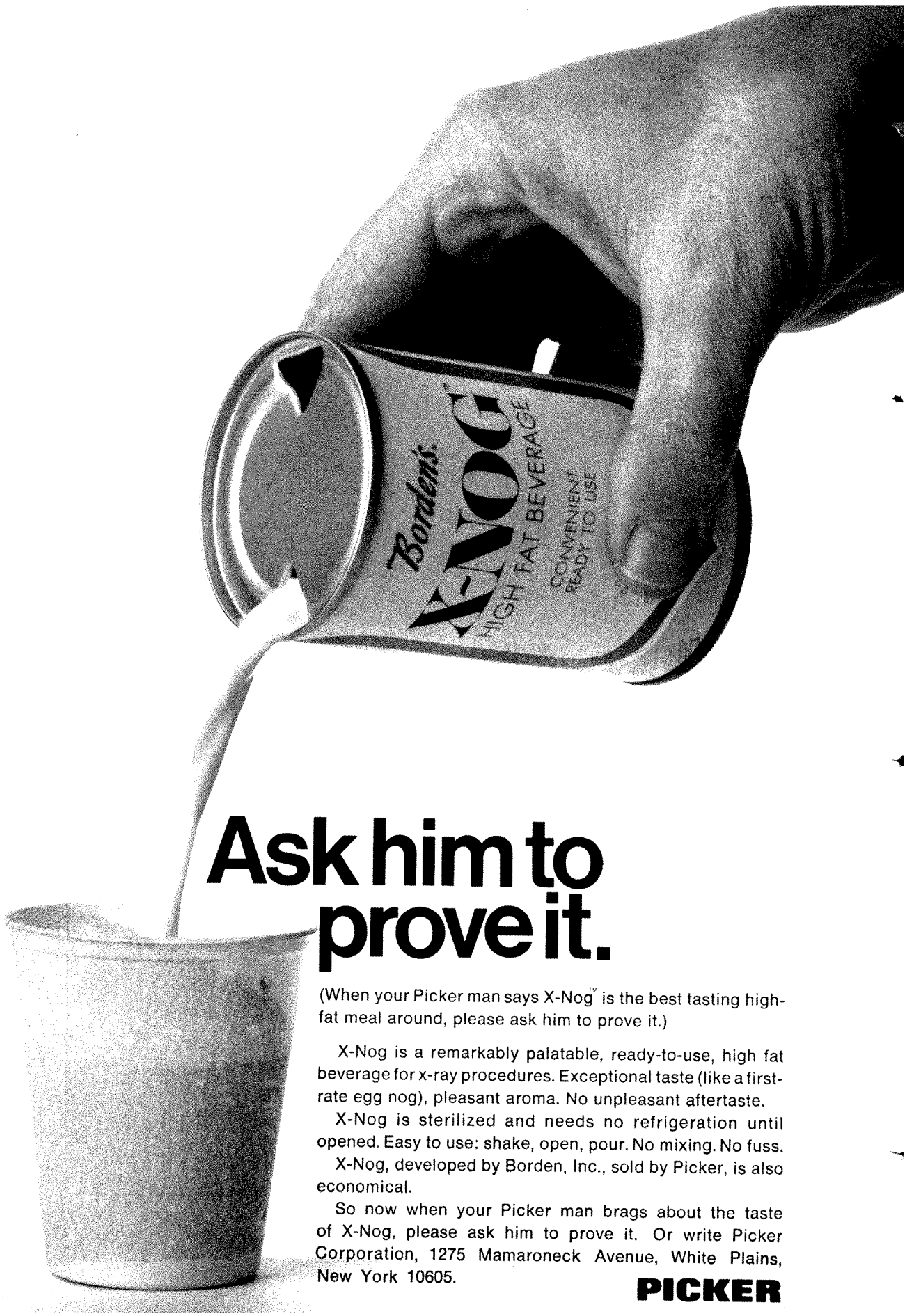
identifying number is fed into the keyboard. Searches up to 1558 folders per second.

Monotrieve, for "medium to low activity" films, codes storage cradle openings rather than individual files. Cradles are stored in face-to-face linear banks arranged as high or as long as space permits. Real space economy. Cradles are scanned, 50 inches per second, then brought by keyboard command to the operator. No walking, reaching or stooping.

Monoscan, Monotrieve — or both systems — can lighten your film handling load. Ask your GE representative how, or write for literature: General Electric, 4855 Electric Ave., Milwaukee, Wis.

GENERAL ELECTRIC





Ask him to prove it.

(When your Picker man says X-Nog™ is the best tasting high-fat meal around, please ask him to prove it.)

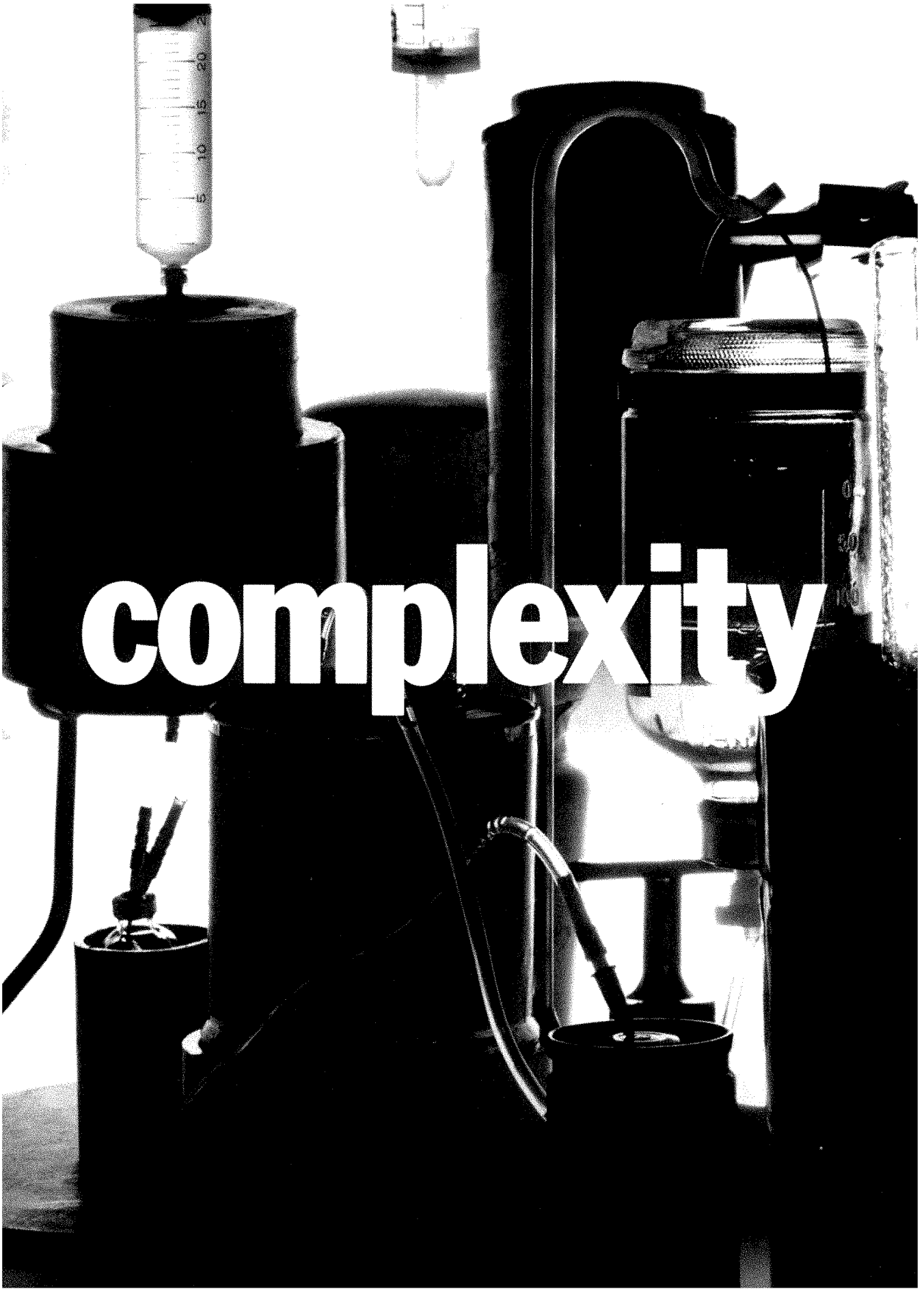
X-Nog is a remarkably palatable, ready-to-use, high fat beverage for x-ray procedures. Exceptional taste (like a first-rate egg nog), pleasant aroma. No unpleasant aftertaste.

X-Nog is sterilized and needs no refrigeration until opened. Easy to use: shake, open, pour. No mixing. No fuss.

X-Nog, developed by Borden, Inc., sold by Picker, is also economical.

So now when your Picker man brags about the taste of X-Nog, please ask him to prove it. Or write Picker Corporation, 1275 Mamaroneck Avenue, White Plains, New York 10605.

PICKER


complexity


simplicity!
TECHNETOPE II
SQUIBB
CAUTION
RADIOACTIVE MATERIAL

SQUIBB
a research concept in nuclear medicine

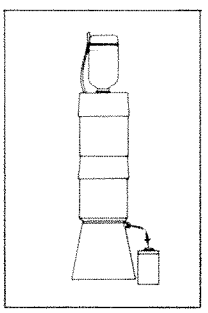
Introducing new Technetope® II

Squibb Technetium 99m STERILE GENERATOR

A FAR SIMPLER GENERATOR . . .
Hooks, hangers, and handles complicate assembly, so you won't find any on Technetope II. It's so simple that, after the usual aseptic techniques, assembly consists basically of two insertions into the generator column. Then attach an eluent bottle, an evacuated collecting vial, and milk. *That's* simplicity.

. . . DESIGNED WITH "T.D.S." IN MIND
Time: Technetope II simplicity reduces assembly time...keeping radiation exposure to a minimum. However, proper radiation safety precautions should be maintained at all times.
Distance: Technetope II allows you to keep your distance. You don't have to be constantly near the generator because it is self-milking. And eluate collection is made *at the side* of the unit—*away* from an unshielded port.
Shielding: Technetope II has another half-value layer of lead shielding—without adding a cumbersome dispenser, additional cost, or special contract.

In addition, Technetope II is readily adaptable to tandem milking which provides high concentrations of ^{99m}Tc per ml.—another Squibb first and exclusive.



Technetope II (Squibb Technetium 99m) Sterile Generator provides a means of obtaining a sterile, non-pyrogenic supply of Technetium 99m (^{99m}Tc). ^{99m}Tc, the short-lived daughter ($T\frac{1}{2} = 6$ hours) of Molybdenum 99 (^{99}Mo, $T\frac{1}{2} = 67$ hours), is obtained from the generator by periodic elution. The amount (in millicuries) of ^{99m}Tc obtained in the initial elution will depend on the original potency of the generator, while the activity obtained from subsequent elutions will depend on the time interval between elutions.

Warning: Proper radiation safety precautions should be maintained at all times. The column containing ^{99}Mo need not be removed from the lead shield at any time. The radiation field surrounding an unshielded column is quite high. Solutions of ^{99m}Tc withdrawn from the generator should always be adequately shielded. The early elutions from the generator are highly radioactive. For radiation protection, a lead shield for the collecting vial is included with Technetope II.

For additional information on this advanced generator or the tandem milking technique, please use the coupon below.

I would like to receive full information on:

☐ **Technetope® II** (Squibb Technetium 99m) Sterile Generator

☐ Tandem Milking with Technetope II

Please attach this coupon to your letterhead and mail to Medotopes Customer Service Dept., P. O. Box #7, East Brunswick, N. J. 08816.

Medotopes®

Squibb Division of Nuclear Medicine
East Brunswick, New Jersey 08816

CLEAR CHOICE IN HYSTEROSALPINGOGRAPHY

WATER-SOLUBLE CONTRAST MEDIUM

SALPIX®

0.53 Gm Sodium Acetrizoate and 0.23 Gm Polyvinylpyrrolidone per cc

Fast, safe, accurate radiopaque visualization without irritation, residue, or pain



ORTHO PHARMACEUTICAL CORPORATION • RARITAN, NEW JERSEY

CONTRAINDICATIONS—Contraindications to hysterosalpingography include the presence of severe vaginal or cervical infections, existing or recent pelvic infection, marked cervical erosion or endocervicitis, and pregnancy. The procedure is contraindicated during the immediate pre- or post-menstrual phase. SENSITIVITY—If indicated in the patient's history, an intracutaneous skin test or sublingual absorption observation may be done with 0.1 cc SALPIX. WARNING—Not for intravenous use.

©OPC 1966

MACHLETT

The Machlett Dynamax "61" X-ray Tube permits the application of direct magnification roentgenography to vascular opacification studies . . . and helps improve diagnostic accuracy.

Conventional arteriogram

Direct serial magnification arteriogram





MACHLETT

The arteriograms on the preceding page demonstrate the increased information available with direct serial magnification compared to routine angiography.

The x-ray tube recommended for making these examinations is the Machlett Dynamax "61", a specialized version of the Dynamax "60". This fine-focus x-ray tube is capable of operating at the higher loadings required for rapid sequential short exposures.

The Dynamax "61" is also designed for high-energy angiography as well as enlargement radiography. In addition, it extends cine-radiographic and spot film capabilities.

Ratings and Characteristics

Maximum Peak Voltage	150 PKV (Anode to cathode)
Anode Heat-Storage Capacity	200,000 HU
Insert Tube Target Angle	10°
Insert Tube Anode	Rotary type with rhenium tungsten faced molybdenum target of high heat-storage and cooling capacity.
Focal Spot Combinations Available	0.3mm small focal spot with 1.0mm large focal spot

Write for a copy of "An Atlas of Serial Magnification Roentgenography," a 32-page booklet containing comparisons of cerebral, vertebral, pulmonary, renal, celiac, mesenteric, hand and wrist arteriograms obtained by direct serial magnification and by conventional techniques. Complete technical information is also available covering the Dynamax "61" tube. The Machlett Laboratories, Inc., 1063 Hope Street, Stamford, Conn. 06907.



RAYTHEON

THE MACHLETT LABORATORIES, INC.

A SUBSIDIARY OF RAYTHEON COMPANY

Director of Radiotherapy and Radiotherapists

Dr. W. W. Cross Cancer Institute

Edmonton, Alberta

Applications are invited for Director of Radiotherapy and qualified Radiotherapists for positions now available in our new Cancer Hospital.

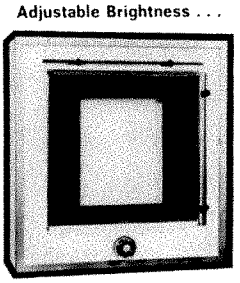
A new 78 bed cancer hospital was completed on July 1, 1968, containing extensive Radio Isotopes, Diagnostic Radiology and Medical Physics departments and other support facilities. The Radiotherapy Department includes two cobalt units, a cecium unit, deep and superficial x-ray units, and a linear accelerator to be installed in several months. Fully modern isotope facilities are available. All malignancies in the Northern half of the Province are referred through the new Cancer Hospital. There is also the opportunity for clinical research.

Effective January 1, 1969, the salary range is $22,000 to $36,000.

There is a superannuation scheme, relocation allowance, Group Life Insurance and other fringe benefits.

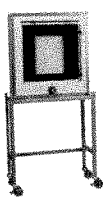
Further information and application forms can be obtained from Dr. J. R. Ibberson, Executive Medical Director, Provincial Cancer Hospitals Board, 11560 University Avenue, Edmonton 61, Alberta, Canada. Telephone collect (403) 433-9461.

Field Collimation and Adjustable Brightness . . . FOR BETTER FILM VIEWING



PHAROS I

INTENSIVE INSPECTION "CURTAINED" ILLUMINATOR: 17x17 in. viewing area with stepless brightness control providing all-over selective collimation down to point size. Distortion-free magnification by powerful two-lens aplanatic optics, weightlessly suspended in front of illuminator . . . (optional, not shown in picture).



MOBILE TABLE STAND
With ball bearing casters and brakes

OTHER P.V.E. PRODUCTS:

- PHAROS "ROTATABLE" ILLUMINATOR: The economic mass viewing device for uninterrupted round-the-clock viewing.
- PHAROS II "TWO-BANK" ILLUMINATOR:
- PHAROS H.I. HIGH INTENSITY ILLUMINATOR: (7 tubes).
- PHAROS SHUTTER ATTACHMENT: For instant conversion of the currently used 14x17 in. curtainless illuminator into a "curtained" one.
- PHAROS "COOL" ILLUMINATOR: A diaphragming spot illuminator for prolonged uninterrupted viewing.
- PHAROS "METRO-LEVEL": A 6½ ft. long roll-up inch and centimeter measuring tape with built-in precision level. A must for the x-ray room.

PHAROS VIEWING EQUIPMENT

FOR ADDITIONAL INFORMATION: Contact your X-ray Supply Company or PHAROS VIEWING EQUIPMENT.
132 MYRTLE AVE., FORT LEE, N.J. 07024

RADIOLOGIST, Board certified or eligible for joint appointment on faculty of Medical College of Georgia and affiliated Dean's Committee, VA Hospital. Special salary arrangements possible. An equal opportunity employer. Contact: Chairman of Radiology Search Committee, LEO G. HORAN, M.D., Veterans Administration Hospital or MARK BROWN, M.D., Chairman, Department of Radiology, Medical College of Georgia, Augusta, Georgia 30904.

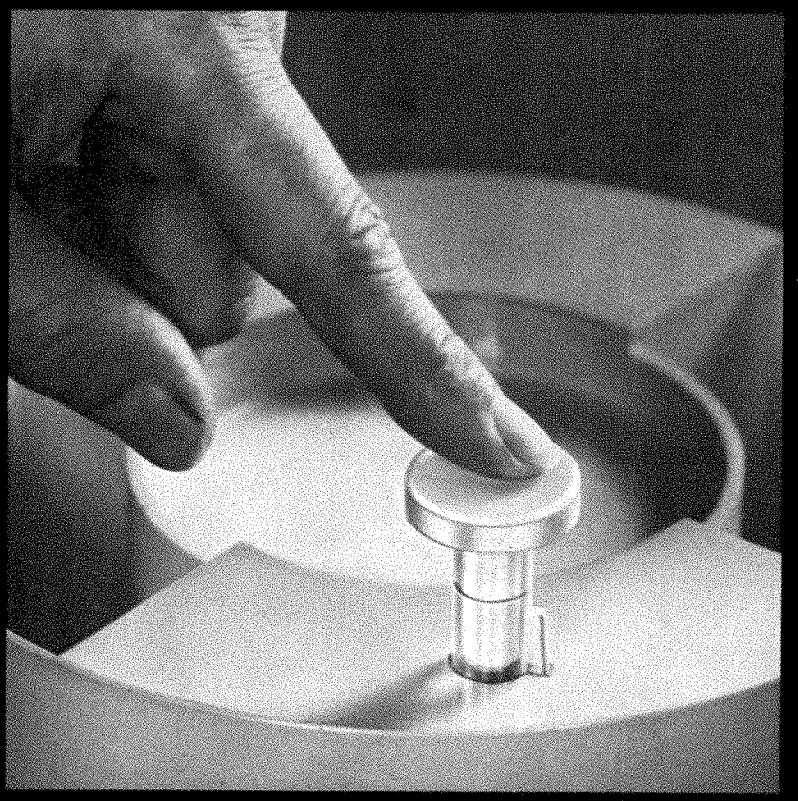
In reply to advertisers please mention that you saw their advertisement in

THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE

• • •

CHARLES C THOMAS
PUBLISHER
Springfield · Illinois

Push Button Milking



New faster way to daily production of ^{99m}Tc in your own laboratory

Ultra-TechneKow® Generator

Simplest way to produce sodium pertechnetate Tc99m
No assembly, no clamps, no generator manipulation.



ONLY 4 STEPS
IN THIS SIMPLE MILKING PROCEDURE

1. Attach sterile needle to plunger outlet.*
2. Place sterile, evacuated vial in elution safe and position it under needle.
3. Press plunger down so needle pierces diaphragm on evacuated vial; turn plunger slightly to lock in position. Milking will proceed automatically.
4. Release plunger to stop milking process. (Vial is now ready for calibration.)

*One needle serves for a full week. For sterility between milkings, retract needle and apply sterile needle cover.

The Mallinckrodt / Nuclear Ultra-TechneKow Generator is so modern, so simple to operate that any other system is antiquated, old fashioned, obsolete.

You receive the complete, plastic-enclosed Ultra-TechneKow Generator each week. No need to handle the generator or make tubing connections. When generator is exhausted, dispose of entire unit or return to Mallinckrodt for disposal.

Available in 4 activities:
50 mc 100 mc 200 mc 300 mc

Ask your Mallinckrodt/Nuclear Salesman for full information, or mail in the coupon.

MALLINCKRODT/NUCLEAR
Box 10172 • Lambert Field
St. Louis, Missouri 63145

Please send complete information on the new Mallinckrodt/Nuclear Ultra-TechneKow Generator.

Name (Please Print) _____

Position or Department _____

Laboratory or Hospital _____

Street _____

City _____ State _____ Zip _____

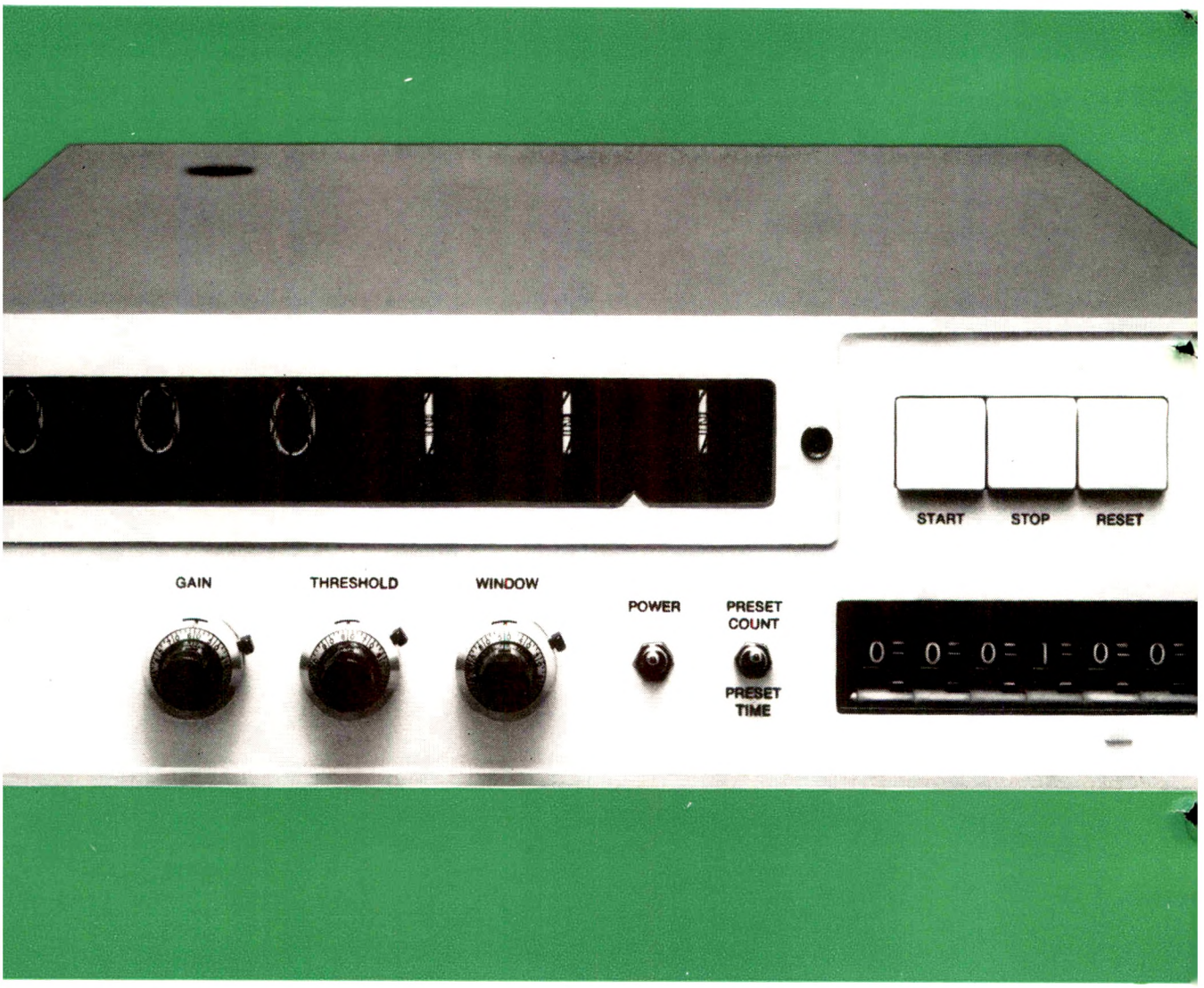
Patent Applied For

Mallinckrodt® NUCLEAR

RADIOPHARMACEUTICALS

MALLINCKRODT CHEMICAL WORKS
Box 10172 • Lambert Field
St. Louis, Missouri 63145
Atlanta • Chicago • Cleveland
Los Angeles • New York • Montreal

Abbott Laboratories is now



This is the
LOGIC™ Well Counter–
only inches larger than this page
(12¼″ x 4 1/16″ x 13″ to be exact)

TM—TRADEMARK

in Nuclear Instruments



The LOGIC Series—the most compact counting systems ever designed—is available now in 3 models.

The LOGIC Counting Systems offer:

804468

- Compactness (micrologic integrated circuitry)
- Dependability (pre-tested for 40 hours)
- Portability (25-35 lbs.)
- Versatility (choice of 3 models)
- Quality (backed by Abbott)

For more information, contact your Abbott man who knows both instruments and radio-pharmaceuticals

ABBOTT LABORATORIES NORTH CHICAGO, ILLINOIS
Abbott Laboratories, S.A., 2, rue Thalberg, 1201 Geneva, Switzerland

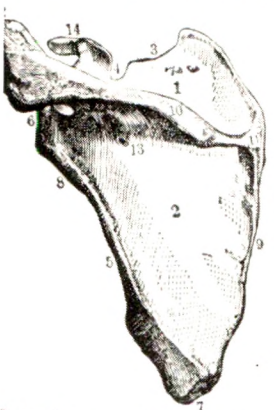
...ska ...fo-hi″dro-sef′ah-
hich the head assumes a

...ska″fo-hi″dro-sef′ah-le).

scaphoides; Gr. *skaphē*
...aped like a boat; navic-
...es: the outer bone of the
...ones. 3. A bone on the
...efore the astragalus and
...ie.

...is). Inflammation of the
s., osteochondrosis of

scapulae [L.]. The shoul-
ular bone in the back of



Scapula, posterior view: 1, spraspinous fossa; 2, infraspinous fossa; 3, superior margin; 4, scapular (coracoid) ...ch; 5, axillary margin; 6, ...noid cavity; 7, inferior an...; 8, neck of the scapula; 9, ...tebral margin; 10, spine; 11, triangular commencement, ...on which the tendon of the ...pezius muscle moves; 12, ...omion; 13, arterial foramen; coracoid process (Leidy).

ula + Gr. *ektomē* exci-
val of the scapula or a

...″u-lo-an-te′re-or). De-
fetus in transverse pre-
la directed anteriorly.

...kap″u-lo-klah-vik′u-lar).
and the clavicle.

...-din′e-ah) [*scapula* + Gr.
...egion of the shoulder.

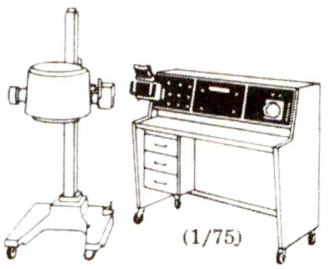
...u-lo-hu′mer-al). Pertain-
...ie humerus.

...pek″se) [*scapula* + Gr.
tion of fixing the scapula
cases of myopathy.

...″u-lo-pos-te′re-or). De-

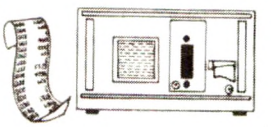
...fever. See under *fever.* **s. angino′sa,** a danger-
ous form with marked throat symptoms.

scintillation camera (sĭn′tĭ-lā′shŭn kăm′ĕr-ă). The Pho/Gamma® III manufactured by Nuclear-Chicago Corporation. Provides in-vivo visualization and recording of radioisotope distribution in body organs through a variety of readout techniques.



(1/75)

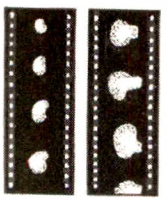
scintidigit (sĭn′tĭ-dĭj′ĭt). Digitized record, on paper tape of total number of counts accumulated during each Pho/Gamma III examining period. Produced by high-speed digital printer accessory.



scintiphoto (sĭn′tĭ-fō′tō). Photographic recording of radioisotope distribution in body organs, as displayed on Pho/Gamma III oscilloscope. Scintiphotos can be either **1.** individual, self-developing pictures exposed during total examination period and processed by triple-lens camera supplied with Pho/Gamma III, or **2.** serial, time-lapse pictures made throughout examination period on 35mm film by optional automatic time-lapse camera available for Pho/Gamma III.

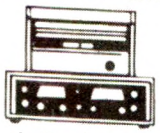


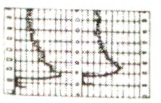
Scintiphoto **1**



Scintiphoto **2**

scintiplot (sĭn′tĭ-plŏt′). Analog record, on chart paper, of radioisotope distribution, as visualized by Pho/Gamma III. Used especially for renal studies, when Pho/Gamma III detector is operated in divided-crystal mode. Produced by dual-channel ratemeter/dual-pen recorder accessory combination.





scintitape (sĭn′tĭ-tāp′). Magnetic-tape recording of Pho/Gamma III data. Produced by magnetic tape system accessory. Clinical information is transferred to tape by system's multidimensional analyzer. Tape is manipulated by system's tape transport. Taped data can be **1.** played back for photographic recording from analyzer's scope as digital scintiphotos (DSP), or **2.** fed to an off-line computer for automatic processing and analysis.



We're helping add some new words to the "diagnostic dictionary."

Because we've come up with some exciting new accessories for the Pho/Gamma® III Scintillation Camera.

Perhaps not all of the words in our "dictionary" will end up in the clinician's vocabulary. Frankly, we invented most of them. For a reason. To help illustrate the newly expanded versatility of Pho/Gamma III for the processing, storage, and analysis of data on radioisotope distribution in body organs and areas.

And versatility *is* the key word. Now Pho/Gamma III can help you learn more, in more ways, than ever before.

For example: To the familiar scintiphoto must now be added *sequential* scintiphotos. They're taken with our new 35-mm automatic time-lapse camera. It fits right on one of the twin scopes on the Pho/Gamma III console.

Other new additions include analog chart records, digital printouts, magnetic tape — all new, all briefly defined in our dictionary.

Why not use it as a point of departure for a talk with your Nuclear-Chicago sales engineer. Or write to us for all of the words on Pho/Gamma III and its expanded array of accessories.

Research in the Service of Mankind

NUCLEAR-CHICAGO CORPORATION

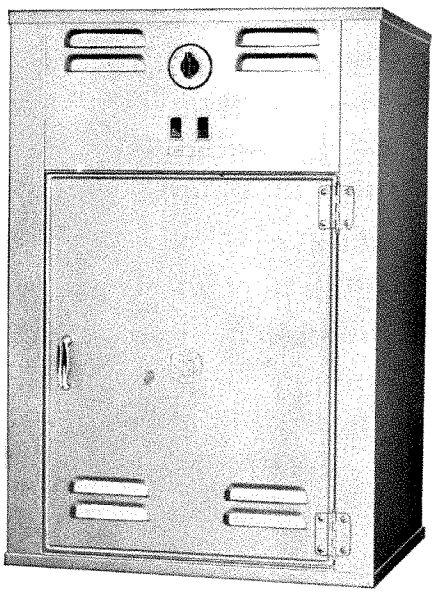
A SUBSIDIARY OF G. D. SEARLE & CO.

307 East Howard Avenue
Des Plaines, Illinois 60018, U.S.A.

Donker Curtiusstraat 7, Amsterdam W.

BUCK X-RAY PRODUCTS

MODEL 50 FILM DRYER



Catalog No. 1050

NOW IN PRODUCTION

ORDER NOW!

SPEED YOUR FILM DRYING

Fast Drying - Economical - 12 Film Capacity

Cabinet Type - 60 Minute Timer - Controlled Heat

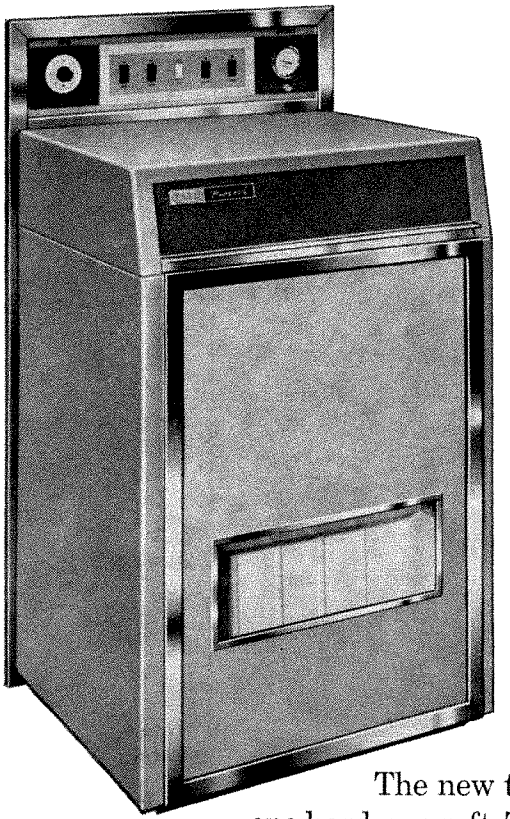
Twin Blower - Recirculating Air

Mist Tan - Mist Green - Standard Gray Green

Order From Your X-Ray Supply Dealer

BUCK X-OGRAPH COMPANY

8709 XOGRAPH AVENUE ST. LOUIS, MISSOURI 63136

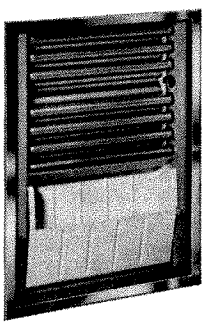


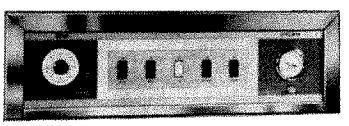
Announcing the Pakorol-XU... the

newest processor for x-ray film... already more than a year old. (*That's how long it has been tested in hospitals, clinics and offices.*) In just a little over 5 square feet of light area, it produces unequalled quality results... in as little as 90 seconds. The Pakorol-XU can be adapted to other standard processes, too.



The new transport system uses paired rollers—one hard, one soft. Their squeegee action eliminates film streaking. The dryer dries films thoroughly at low temperature—a must for quality RP film. It eliminates heat marking. For the operator's convenience, controls are on an eye-level panel. And to really simplify maintenance, all plumbing and electrical components are easily accessible by removing one panel below the feed table.





There's much more. If you (or your department) process radiographs, you must see the new Pakorol-XU. Ask your Pako Distributor or send the coupon for more information.

PAKO CORPORATION PAKO®
6300 Olson Memorial Highway, Minneapolis, Minnesota 55440
PS Processing Systems for the Photographic, Graphic Arts, Motion Picture, Medical and Industrial X-Ray Industries.

PAKO CORPORATION
6300 Olson Memorial Hwy. • Minneapolis, Minn. 55440

Please rush me complete information on the New Pakorol-XU

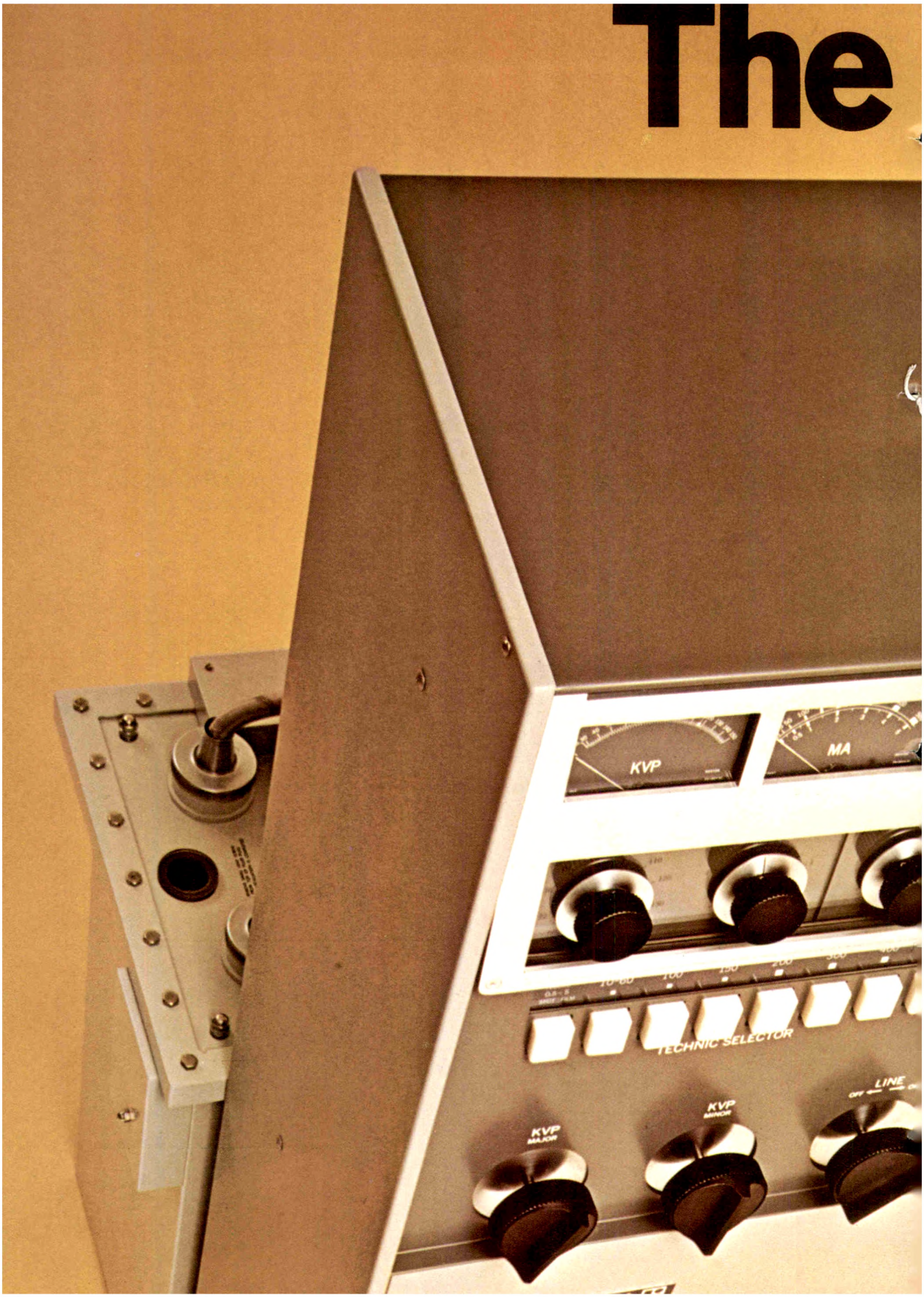
Hosp/Clinic/Office_____

ADDRESS_____

CITY_____ STATE_____ ZIP_____

NAME_____

The



Lightweight.



Some people seem to think x-ray generators should be sold by the pound. That if one backup circuit is good, then three make it even better.

Nonsense.

The more spaghetti you put inside one of these things, the more you've got that can go wrong with it. Excess circuitry leads to just one result: excess downtime.

So this Profexray generator—and all our other equipment—is engineered to cut out electronic redundancy. Of course, all the necessary backup systems are there. But it's a little lighter in weight than most. And one heck-of-a-lot more reliable.

Notice too, please, that our transformer isn't chubby like all the others. Which makes it fit handily under a cabinet somewhere, instead of in the basement.

Before you buy or specify any new equipment, let us show you the muscle in one of our lightweights.

Without an ounce of fat.

Litton Medical Products
A Litton Industries Group, Profexray Division
515 East Touhy Avenue — Des Plaines, Illinois 60018

Improved reliability, even better performance.

Ohio Nuclear's new Model 84FD Dual Five, is the only scanner employing reliable, digital logic, computer-type electronics.

Speeds up to 750 cm./minute produce simultaneous, opposed view photoscans in less than half the time required by other scanners.

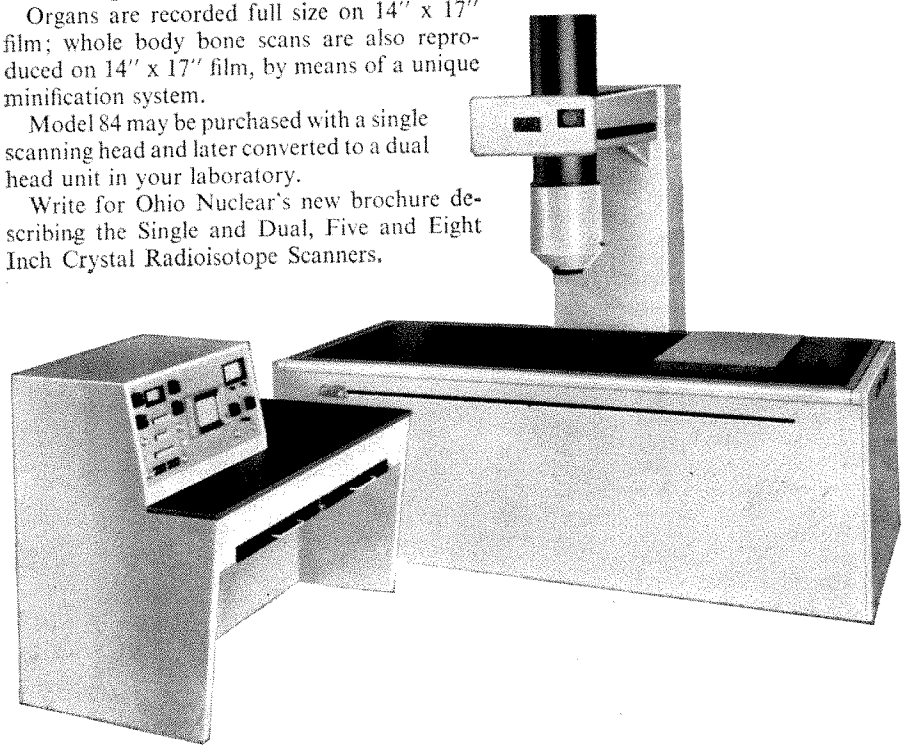
Scan progress is visually monitored on a storage cathode ray tube, which retains the organ image until manually erased.

Simplified pushbutton controls are conveniently located on the desk console. Photo Intensity Computer (PIC) circuit provides consistent, comparable maximum film density at the push of a button. Selectable levels of contrast enhancement and background erase accommodate individual preference.

Organs are recorded full size on 14" x 17" film; whole body bone scans are also reproduced on 14" x 17" film, by means of a unique minification system.

Model 84 may be purchased with a single scanning head and later converted to a dual head unit in your laboratory.

Write for Ohio Nuclear's new brochure describing the Single and Dual, Five and Eight Inch Crystal Radioisotope Scanners.



ohio-nuclear, inc.

1725 Fall Avenue, Cleveland, Ohio 44113 (216) 621-8142

Bright-image fluoroscopy on wheels.

Picker's "Surveyor" lets you wheel the best in fluoroscopy to any needed location. At the bedside, in the emergency or operating room, in the coronary care suite... wherever you find a standard 110 V, 20 amp. outlet . . . you can have the advantages of modern image-intensified fluoroscopy.

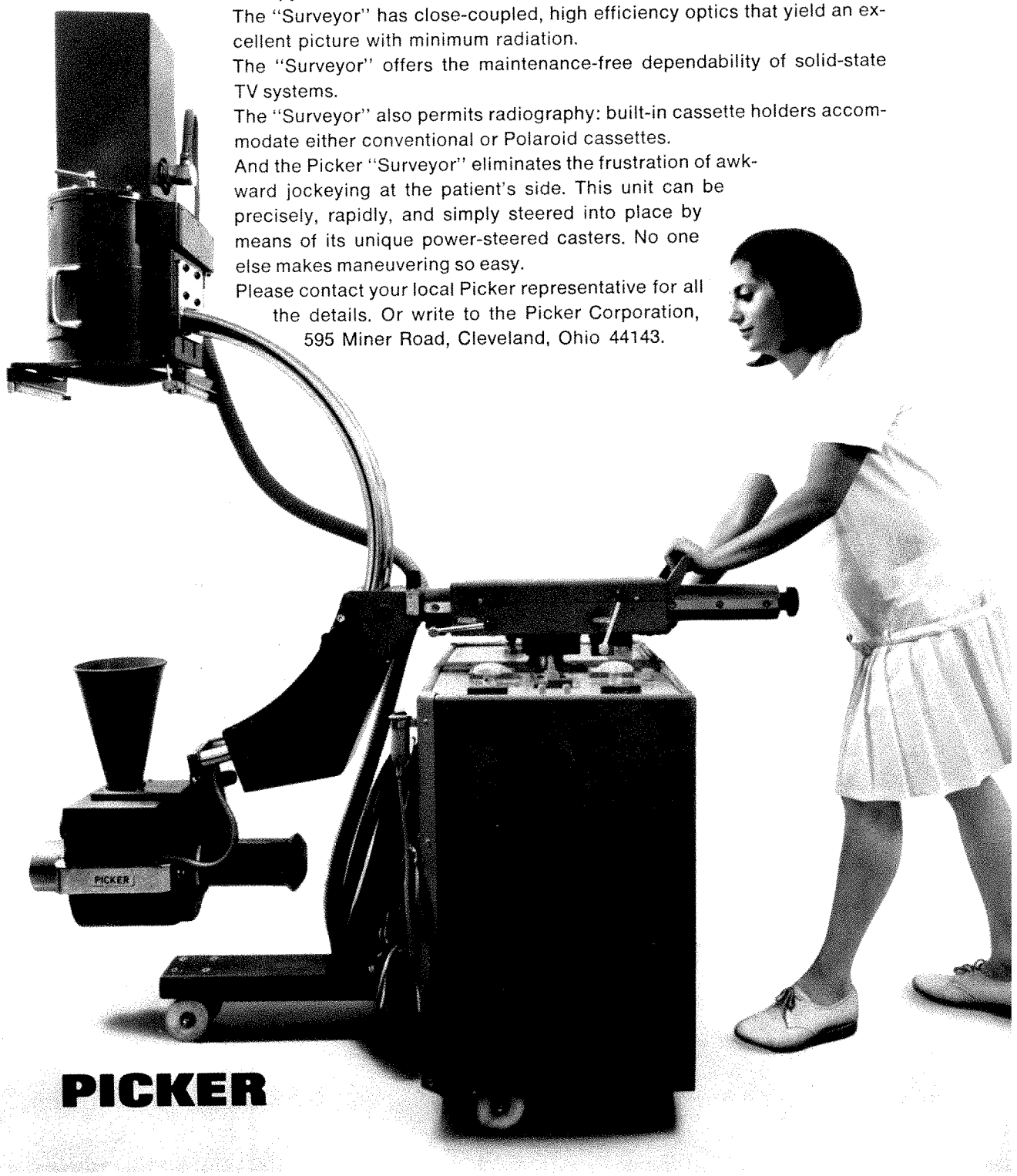
The "Surveyor" has close-coupled, high efficiency optics that yield an excellent picture with minimum radiation.

The "Surveyor" offers the maintenance-free dependability of solid-state TV systems.

The "Surveyor" also permits radiography: built-in cassette holders accommodate either conventional or Polaroid cassettes.

And the Picker "Surveyor" eliminates the frustration of awkward jockeying at the patient's side. This unit can be precisely, rapidly, and simply steered into place by means of its unique power-steered casters. No one else makes maneuvering so easy.

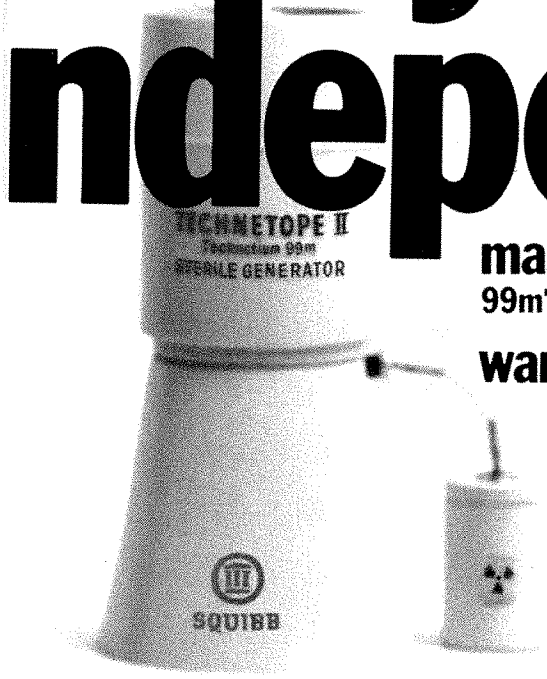
Please contact your local Picker representative for all the details. Or write to the Picker Corporation, 595 Miner Road, Cleveland, Ohio 44143.

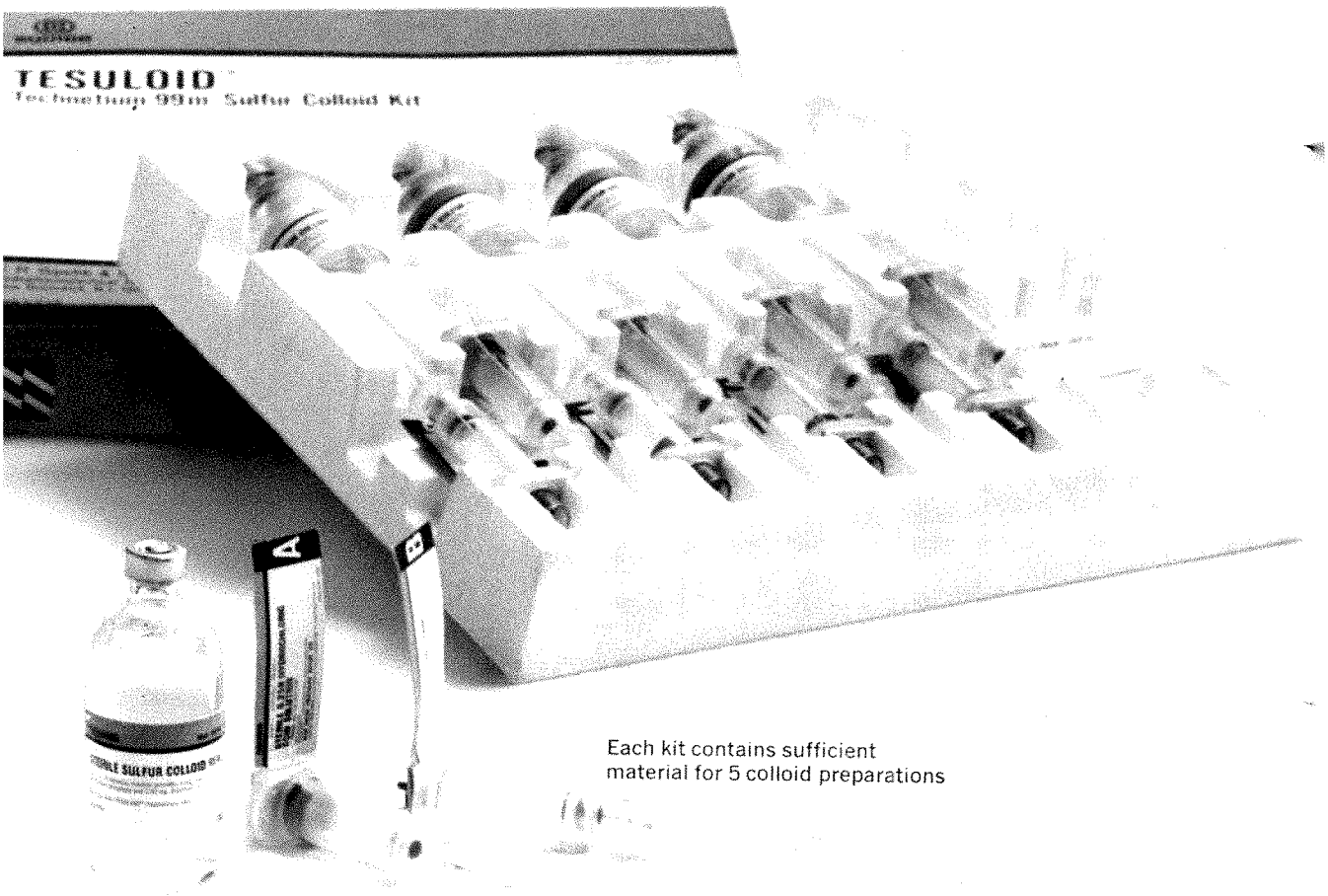


PICKER

oday be ndependent!

make your own ^{99m}Tc Sulfur Colloid when you want it...when you need it





Each kit contains sufficient material for 5 colloid preparations

Tesuloid™

Technetium 99m–Sulfur Colloid Kit

...utilize ^{99m}Tc eluate from your sterile generator
...make as many doses as you want when you want
...keep dollar loss from product decay to a minimum
...more convenient and economical
...store kit anywhere – it's not radioactive*
...colloid contains no dextran...no rhenium

Package contains:

5 vials (3 cc. each) Sterile Sulfur Colloid Reaction Mixture. Each cc. of aqueous solution provides 4 mg. sodium thiosulfate, 3 mg. gelatin, 8.5 mg. potassium phosphate and 0.93 mg. disodium edetate. Contains no preservative.

5 UNIMATIC® Disposable Syringes (2 cc. each) of Sterile 0.25N Hydrochloric Acid Solution. Each cc. of aqueous solution provides 9 mg. hydrochloric acid.

5 UNIMATIC Disposable Syringes (2 cc. each) of Sterile Buffer Solution. Each cc. of aqueous solution provides 35 mg. sodium biphosphate and 10 mg. sodium hydroxide.

Warning: Solutions of sodium pertechnetate ^{99m}Tc withdrawn from the generator should always be adequately shielded. Early elutions from the generator are highly radioactive.

Precaution: Radiopharmaceuticals should not be administered to pregnant women or patients under 18 unless the information to be gained outweighs the hazards.

*However, adequate shielding of the Technetium 99m—Sulfur Colloid solution should be maintained.

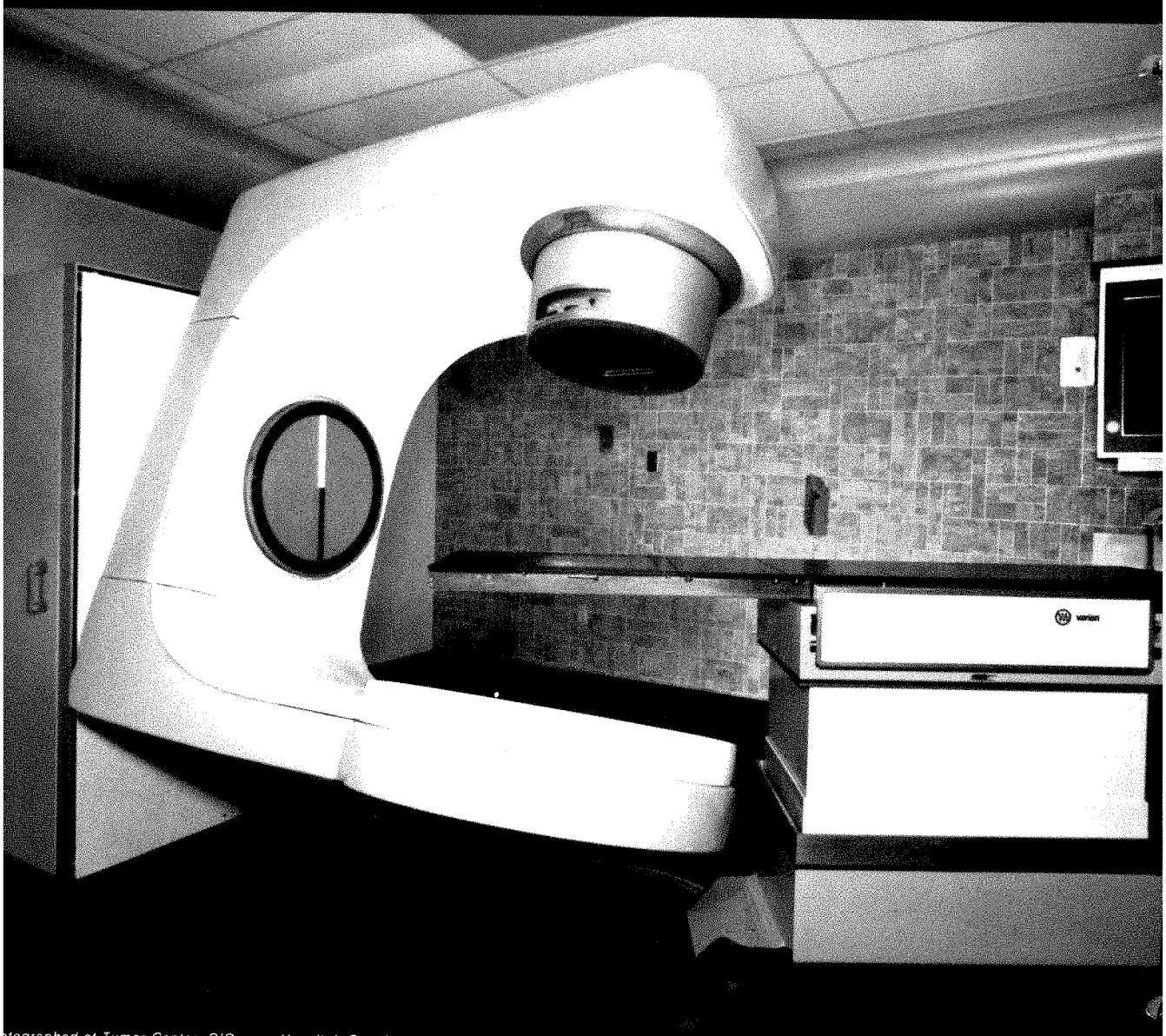
Please send me complete information on new **Tesuloid**™ Technetium 99m—Sulfur Colloid Kit.

Please attach this coupon to your letterhead and mail to Medotopes Customer Service Department, P.O. Box #7, East Brunswick, New Jersey 08816.

Medotopes®

SQUIBB Division of Nuclear Medicine
East Brunswick, New Jersey 08816

Winning an award was not the object of Clinac® 4's grand design.



otographed at Tumor Center, O'Connor Hospital, San Jose, California

A simple, reliable, high-output treatment system was.

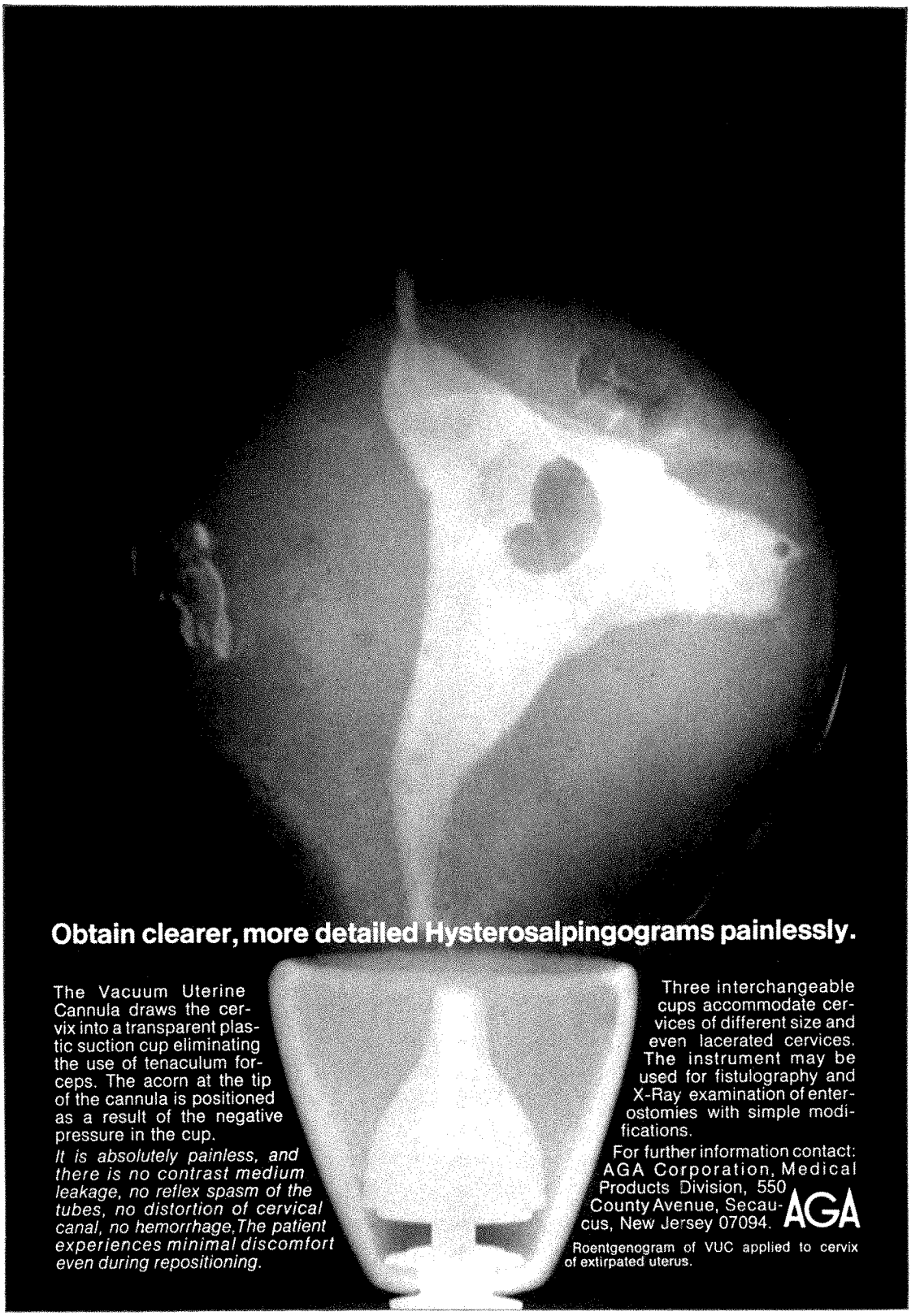
The Clinac 4 linear accelerator was conceived to be the most advanced deep radiotherapy system of our time. As an operational reality, it now is fulfilling this promise. With an output of 350 Rads/min. in field sizes up to 32x32 cm. Providing the uniform high intensity that enables "mantle" treatments to be completed with ease in 2 to 3 minutes.

We thank the judging panel of WESCON for their award. If it now serves to spotlight Clinac 4's contribution to the war on cancer, they will have earned the gratitude of many others.



Twenty-two Clinac 4's are now on order. For further information, contact Varian Radiation Division, 611 Hansen Way, Palo Alto, California 94303; Springfield, New Jersey 07081; Varian A.G., Zug, Switzerland.

varian
radiation
division


Obtain clearer, more detailed Hysterosalpingograms painlessly.
The Vacuum Uterine Cannula draws the cervix into a transparent plastic suction cup eliminating the use of tenaculum forceps. The acorn at the tip of the cannula is positioned as a result of the negative pressure in the cup.
It is absolutely painless, and there is no contrast medium leakage, no reflex spasm of the tubes, no distortion of cervical canal, no hemorrhage,The patient experiences minimal discomfort even during repositioning.
Three interchangeable cups accommodate cervices of different size and even lacerated cervices. The instrument may be used for fistulography and X-Ray examination of enterostomies with simple modifications.
For further information contact: AGA Corporation, Medical Products Division, 550 County Avenue, Secaucus, New Jersey 07094.
AGA
Roentgenogram of VUC applied to cervix of extirpated uterus.

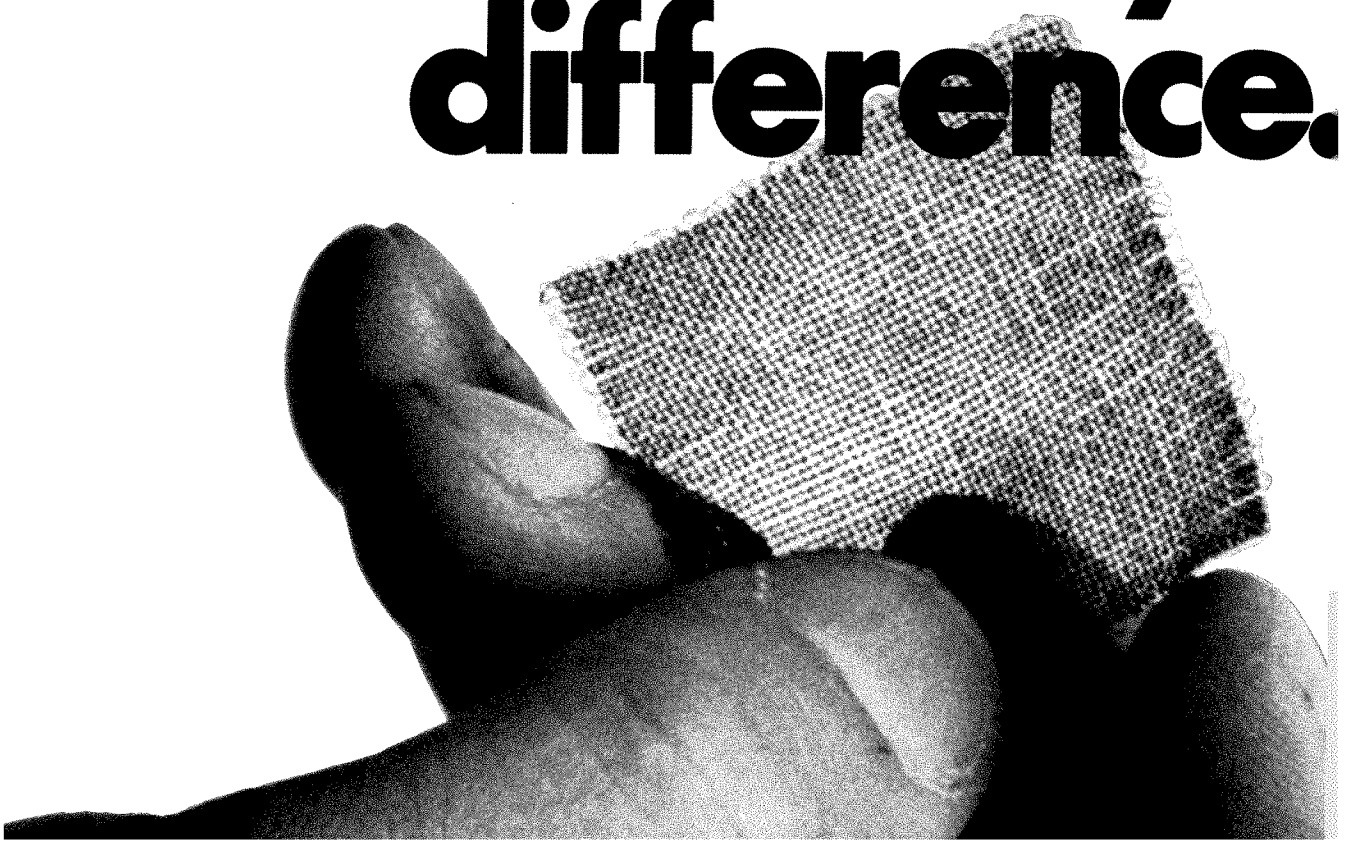
Unlike other scintillation cameras, Baird-Atomic's Autofluoroscope features computer-type memory. And that's saying a lot.

It says our non-volatile magnetic core memory can store raw digital data for each picture element. And *resto* image plane uniformity. It lets you flag any areas of the picture for numerical integration in dynamic studies. permits fast storage on magnetic tape to provide more data points in dynamic studies. It lets you play back patie data in its original form at any time. Instantly. And because of magnetic co memory, the picture has the same integrity as the raw data. The fact is, magne core storage makes the Autofluoroscope a fundamentally more practical and o jective tool. What's more, it's faster and easier to use in all procedures than oth cameras. So if you're going to buy or lease an imaging device, you should talk Baird-Atomic before you make your final decision. You owe it to yourself to fu understand why the tiny difference will make such a big difference to your pr gram. Naturally, if you're not already thinking about the Autofluoroscope, we m not change your mind. But we'll give you a tough decision make. Call for an appointment. 33 University Road, Cambridg Massachusetts 02138, Telephone: 617 864-7420. Baird-Atom Europe, The Hague, The Netherlands. Baird-Atomic Limited, Hornchurch, England.



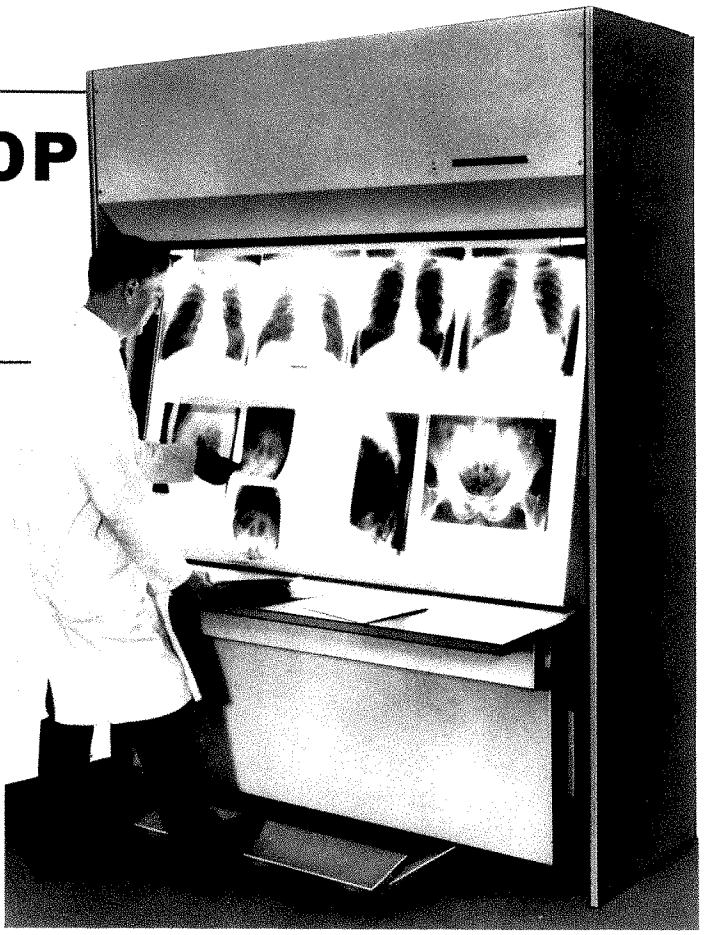
BA BAIRD-ATOMIC

The tiny difference.



ROLLOSKOP

HIGH-CAPACITY FILM VIEWING DEVICE



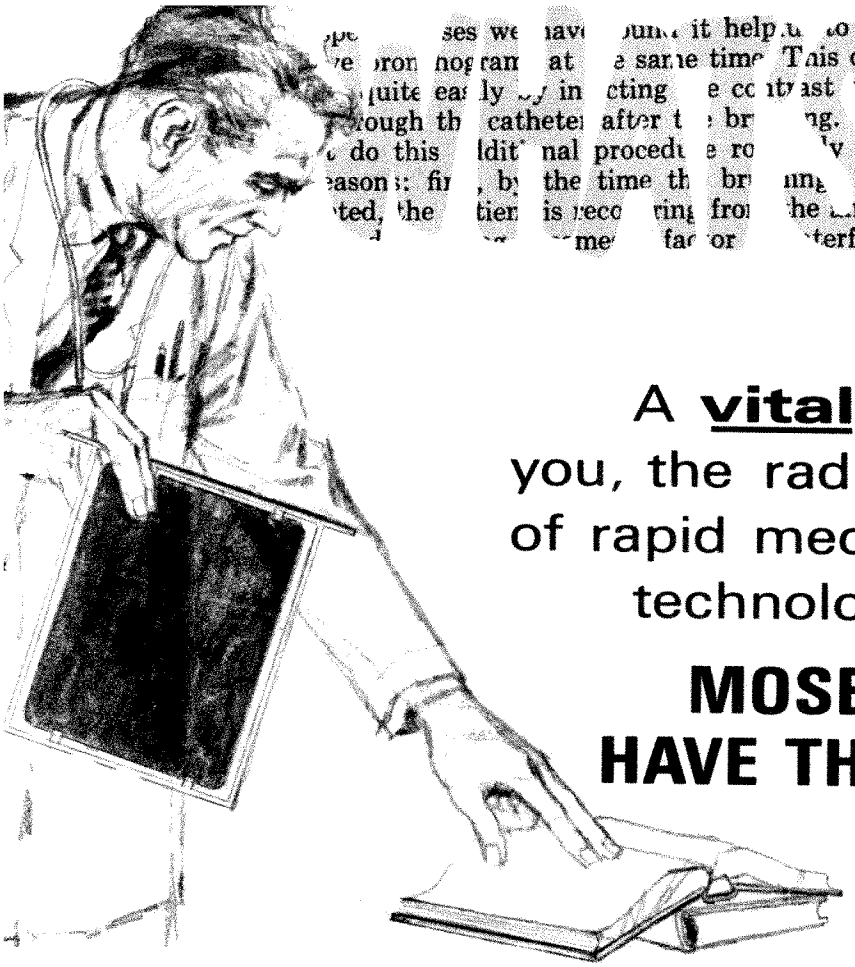
The Rolloskop introduces a time and work saving method for the display of the X-ray films. It is based on a stationary illuminator unit and a mobile carriage for storage and transport of previously hung films. Identical units should be installed in pre-reading and demonstration rooms.

Immediately after processing, the radiographs for reading are hung on a transparent plastic band provided with clips. This band runs vertically over the illuminated area (57″ × 40″) on to spools in the top of the illuminator unit and in the carriage. The carriage with the films can be disengaged from the illuminator and transported to the viewing room where it is engaged to a second illuminator. Thus the films can be demonstrated in different places without being hung more than once. Radiographs can also be kept in spare carriages, e.g. for teaching purpose. Each spool takes up to 160 14″ × 17″ films.



ELEMA-SCHONANDER, INC.

Post Office Box 130 Mount Prospect, Illinois 60056



A **vital** question for you, the radiologist, in an era of rapid medical advance and technological change

MOSBY BOOKS HAVE THE ANSWERS

❶ **THERAPEUTIC RADIOLOGY: Rationale, Technique, Results,** *New 3rd Edition: By William T. Moss, M.D., and William N. Brand, M.D.* Thorough evaluation and revision make this popular book even more valuable to you. Emphasis remains on the rationale of radiotherapy, and the concise, clinically oriented discussions incorporate current concepts. Specific additions include new chapters on "The Heart and Blood Vessels" and "The Prostate Gland", new discussions on tumors of the orbit and lacrimal glands, and many new illustrations throughout. April, 1969. Approx. 576 pages, 303 illustrations. **About $22.50.**

❷ **LUNG CANCER: A Study of 5000 Memorial Hospital Cases,** *New: Edited by William L. Watson, M.D.* Vital information on a vital disease. 31 specialists evaluate material from 5000 cases over the past 40 years. Comprehensive discussions include: radiographic diagnosis, the radiographic appearance of different tumor types, and such new techniques as nuclear radiology and ultrasound; and radiation therapy in lung cancer including interstitial implantation of radioactive seeds. Step-by-step surgical procedures illustrated by Shirley Baty. December, 1968. 602 pages, 454 illustrations, 4 in color. **$29.50.**

ORDER YOUR BOOKS NOW!

FIRST CLASS
PERMIT No. 135
ST. LOUIS, MO.

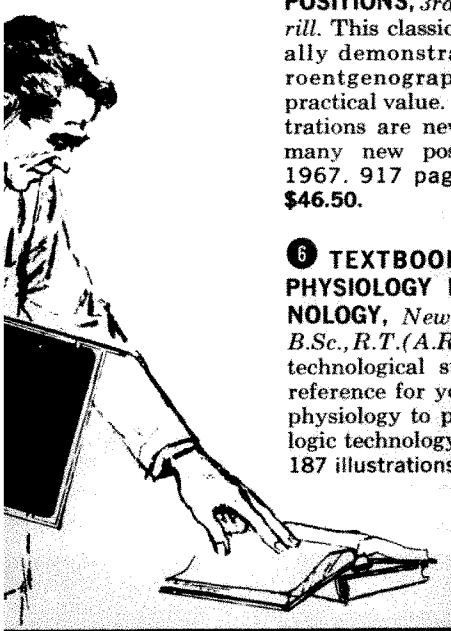
BUSINESS REPLY MAIL
NO POSTAGE STAMP NECESSARY IF MAILED IN THE UNITED STATES

POSTAGE WILL BE PAID BY

The C. V. MOSBY Company
3207 Washington Boulevard
St. Louis, Missouri 63103

MOSBY

Timely Mosby books give new insights into radiologic theory and practice



3 PULMONARY EMPHYSEMA AND RELATED LUNG DISEASES, *New: By Theodore Rodman, M.D., and Francis H. Sterling, M.D.* As the incidence of obstructive pulmonary disease increases, its prompt recognition and treatment grow more and more important. Two distinct sections of this authoritative new book cover "Diagnosis and Pathogenesis" and "Treatment". The former includes an excellent chapter on "Roentgen Manifestations of Pulmonary Emphysema and Chronic Bronchitis". January, 1969. 486 pages, 294 illustrations. **$27.50.**

4 RADIOLOGIC DIAGNOSIS IN INFANTS AND CHILDREN: *By Armand E. Brodeur, M.D., M.Rd., F.A.C.R.* Valuable aid through complexities of pediatric conditions. Shows normal anatomy and physiology, congenital and acquired abnormalities of all organ systems and skeleton of the child. Pinpoints "pitfalls" in diagnosis and how to avoid them. 1965. 515 pages, 757 illustrations. **$26.50.**

5 ATLAS OF ROENTGENOGRAPHIC POSITIONS, *3rd Edition: By Vinita Merrill.* This classic 3-volume atlas graphically demonstrates every conceivable roentgenographic position proven of practical value. 409 of the excellent illustrations are new to this edition, as are many new positions and procedures. 1967. 917 pages, 2142 illustrations. **$46.50.**

6 TEXTBOOK OF ANATOMY AND PHYSIOLOGY IN RADIOLOGIC TECHNOLOGY, *New: By Charles A. Jacobi, B.Sc., R.T.(A.R.R.T.)* A "must" for your technological staff; a convenient quick reference for you. Relates anatomy and physiology to practical, everyday radiologic technology. April, 1968. 439 pages, 187 illustrations. **$12.00.**

7 ALIMENTARY TRACT ROENTGENOLOGY, 2 Volumes: *Edited by Alexander R. Margulis, M.D., and H. Joachim Burhenne, M.D.* Definitive work on x-ray diagnosis of the gastrointestinal tract important to every radiologist. Monumental book discusses examination, diagnosis, techniques, and patient care of all alimentary tract sites. More than 1,400 clear, pertinent illustrations augment the text. 1967. 1231 pages, 1414 illustrations. **$65.00.**

8 COMPREHENSIVE REVIEW FOR THE RADIOLOGIC TECHNOLOGIST, *New: By Matthew Stevens, R.T., and Robert I. Phillips, R.T., FARST.* Provide a convenient reference and review for your technological personnel. Concise question-and-answer format. Excellent review for registry exams. October, 1968. 191 pages, 13 illustrations. **$7.25.**

9 PATIENT CARE AND SPECIAL PROCEDURES IN RADIOLOGIC TECHNOLOGY, *New 3rd Edition: By John C. Watson, R.T.* Your technologists must often deal with desperately ill patients and complex technical situations. Thoroughly revised new edition can help them effectively handle these special radiologic examinations. January, 1969. 248 pages, 146 illustrations. **$8.25.**

10 TEXTBOOK OF RADIOLOGIC TECHNOLOGY, *New 4th Edition: By Charles A. Jacobi, B.Sc., R.T.(A.R.R.T.); and Don Q Paris, R.T.(A.R.R.T.)* Provides quick answers to technical questions on chemistry, physics, darkroom procedures. The most current instructions for technologists on preparation of the patient; "technical tips" from the authors' experience; surgical cholangiography. July, 1968. 499 pages, 384 illustrations. **$12.75.**

COMPLETE COUPON BELOW AND MAIL TODAY

plete, detach and mail today—no stamp required.

The MOSBY GUARANTEE OF SATISFACTION

YOU can determine, after careful cover-to-cover examina-
whether a particular book can benefit you in your profession-
eer. Therefore, each book listed here may be ordered on 30-
pproval. If any book does not live up to your expectations,
ly return it to The C. V. Mosby Company for full credit or
id within 30 days after date of shipment.

PLEASE PRINT

SS

Please send me on 30-day approval the book(s) whose number(s) I have circled below:

1 Moss, THERAPEUTIC RADIOLOGY, about $22.50
2 Watson, LUNG CANCER, $29.50
3 Rodman-Sterling, PULMONARY EMPHYSEMA AND RELATED LUNG DISEASES, $27.50
4 Brodeur, RADIOLOGIC DIAGNOSIS IN INFANTS AND CHILDREN, $26.50
5 Merrill, ATLAS OF ROENTGENOGRAPHIC POSITIONS, $46.50
6 Jacobi, TEXTBOOK OF ANATOMY AND PHYSIOLOGY IN RADIOLOGIC TECHNOLOGY,
7 Margulis-Burhenne, ALIMENTARY TRACT ROENTGENOLOGY, 2 volumes, $65.00
8 Stevens-Phillips, COMPREHENSIVE REVIEW FOR THE RADIOLOGIC TECHNOLOGIST, $7.25
9 Watson, PATIENT CARE AND SPECIAL PROCEDURES IN RADIOLOGIC TECHNOLOGY, $8.25
10 Jacobi-Paris, TEXTBOOK OF RADIOLOGIC TECHNOLOGY,

A recommended course of action for the buyer of radiopharmaceuticals:

1 **INTROSPECTION. Think for a moment. What's your prime concern when you're ready to buy radiopharmaceuticals? Purity? Stability? Availability? Service? Which of these are important to you? Sort them out. Write them down. Give them an order of importance.**

No matter what your analysis reveals, Amersham/Searle Corporation is more than likely to have the solutions. Our range of compounds is wide—from arsenic-74 to xenon-133. Imaging agents for in-vivo investigations. Compounds for in-vitro studies. All with purity and stability of the highest order. All for prompt delivery.

2 **INVESTIGATION. Next, look into the credentials of the suppliers of radiopharmaceuticals. What have they done? What are they doing—in research, in involvement with the field of nuclear medicine itself?**

When you look into Amersham/Searle, the facts are these: A company formed as a joint venture of The Radiochemical Centre, Amersham, England, and G. D. Searle & Co. An organization capable of drawing on the resources of The Centre for radiopharmaceutical research and manufacture. A manufacturer able to utilize the resources of G. D. Searle & Co., a firm long experienced in pharmaceutical research. And a resourceful enterprise capable as well of benefiting from an exchange of information with Nuclear-Chicago Corporation (a Searle subsidiary), designers and manufacturers of nuclear instrumentation.

3 **INFORMATION. Ask to see all available information on the compounds you're interested in. What does the supplier have to say about the radiopharmaceutical? How is it said?**

A Radiopharmaceutical Bulletin from Amersham/Searle is a detailed compilation of facts on every aspect of the compound offered. Clinical information. Biochemical and chemical data. Complete specifications. And extensive bibliographies. Every radiopharmaceutical we make gets the same treatment in our Bulletins.

4 **DECISION: Once you have decided on your probable source of radiopharmaceuticals, make your move. Ask for proof of performance.**

Your phone call or written request to Amersham/Searle will start things moving. We will send complete data on any radiopharmaceutical or attempt to answer any and all questions that go beyond such data. And we'll send you a list of our Telex-connected sales offices. After all, you would expect our actions to speaker louder than our words.

2000 NUCLEAR DRIVE DES PLAINES, ILLINOIS 60018 TELEPHONE: (312) 296-1055



Amersham/Searle

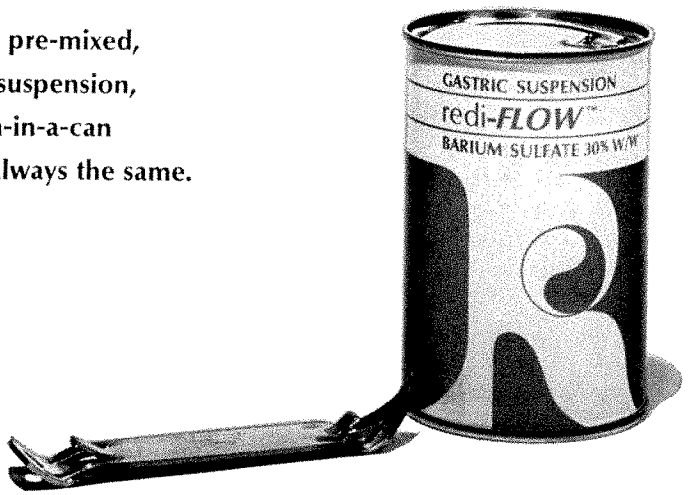
AMERSHAM/SEARLE CORPORATION:
AN ACTIVITY OF G. D. SEARLE & CO. AND THE RADIOCHEMICAL CENTRE

8-216

No two ways about redi-FLOW™

(Gastric Suspension Barium Sulfate 30% w/w)

It's the pre-mixed,
stable suspension,
barium-in-a-can
that's always the same.



No two ways about **redi-FLOW™** (gastric suspension barium sulfate). It's always the same. Get the picture you want with the same patient at later dates because there is no variable factor in the mixing. **redi-FLOW™** (gastric suspension barium sulfate) is always ready-made to the same specifications of barium content, of specific gravity, of suspension, and of flow properties—day after day, month after month. It flows evenly as a consistent, uniform column of barium—doesn't precipitate in gastric fluid or small bowel. Your patients will love it. But don't let them have *all* the pleasure . . . try some yourself . . . it tastes like a good milkshake. No two ways about it—you'll like **redi-FLOW™** (barium sulfate suspension). Test it by using the coupon.

FLOW PHARMACEUTICALS, Inc.
Subsidiary of Flow Laboratories, Incorporated
1070 Linda Vista Avenue, Mountain View, California 94040

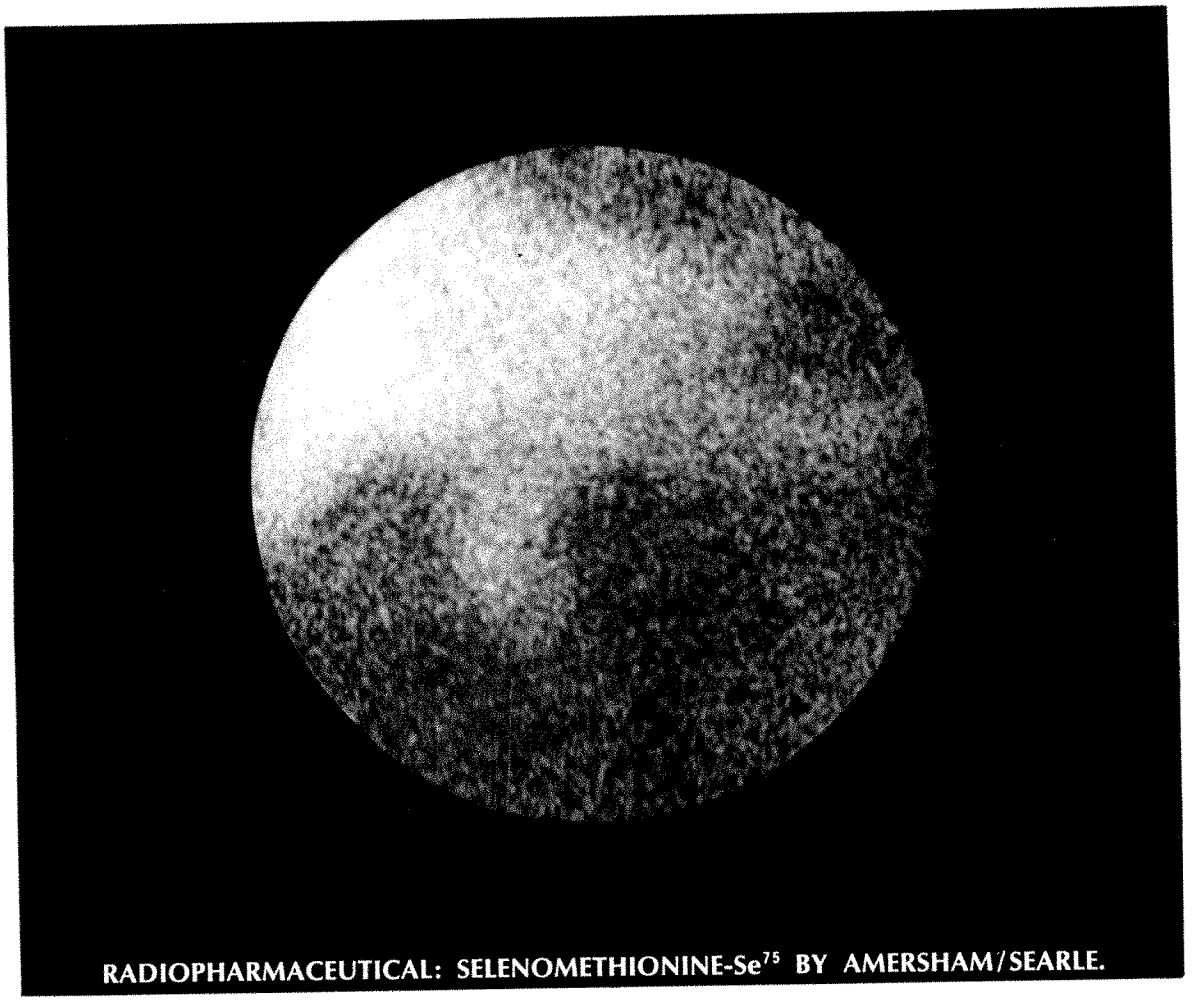
Send **redi-FLOW™** (gastric suspension barium sulfate , 30% w/w) samples to:

Name _____

Address _____

City _____ State _____ Zip _____

Portrait of a Pancreas.



RADIOPHARMACEUTICAL: SELENOMETHIONINE-Se^{75} BY AMERSHAM/SEARLE.

There are many problems inherent in diagnosing diseases of the pancreas by standard radiographic techniques. Further, laboratory determinations are often inconclusive.

Question: Can pancreatic pathology be ruled out as a possible diagnosis short of exploratory surgery?

Answer: Amersham/Searle Corporation now offers the clinician selenomethionine-Se^{75}—a diagnostically reliable imaging agent, especially when used with the gamma scintillation camera for rapid, continuous scintiphotography.

Amersham/Searle's selenomethionine-Se^{75} is of unsurpassed purity and stability. And these qualities are vital to your selection of a drug for your patients. Here are the important specifications for selenomethionine-Se^{75} as supplied by Amersham/Searle:

Stability: Little evidence of radiation decomposition after storage for up to 4 months at room temperature in concentrations of 1 mCi/ml.

Radiochemical purity: >95%.

Chemical purity: >90%.

For further clinical, biochemical, and technical information on L-selenomethionine-Se^{75} (sterile aqueous solution) please write for *Radiopharmaceutical Bulletin RP-1*. Or call us directly.

Indications: Pancreas imaging. **Contraindications:** Radioisotopes should not be administered to patients under 18 years of age, or to pregnant or nursing women, unless invaluable diagnostic information cannot be otherwise obtained. **Precautions:** Observe appropriate radiation-safety procedures at all times. **Availability:** Sterile aqueous solution. Specific activity ranges from 1 to 6 mCi/mg. Radioactivity concentration approximately 250 μCi in 1 ml.

Scintiphoto courtesy D. Bruce Sodee, M.D., Doctors Hospital, Cleveland, Ohio.

2000 NUCLEAR DRIVE DES PLAINES, ILLINOIS 60018 TELEPHONE: (312) 296-1055

Amersham/Searle

AMERSHAM/SEARLE CORPORATION
AN ACTIVITY OF G. D. SEARLE & CO. AND THE RADIOCHEMICAL CENTRE

8-214



MEDICAL SYSTEMS

Information ...anywhere.

You name it: in surgery, emergency, orthopedic and cast rooms. Cardiac monitoring areas. Intensive care suites. The radiology department. Rush it in, roll it up close—and shoot—for precise, clear fluoroscopy and radiography. Information you must have. Anywhere.

That's the GE Mobile Fluoricon® image intensifier. Radiological/surgical teams can localize foreign bodies or guide orthopedic surgery through repeated fluoroscopic views at various angular positions. The unit switches automatically to radiographic levels of radiation when the cassette is inserted, returns to fluoroscopic levels when it's removed.

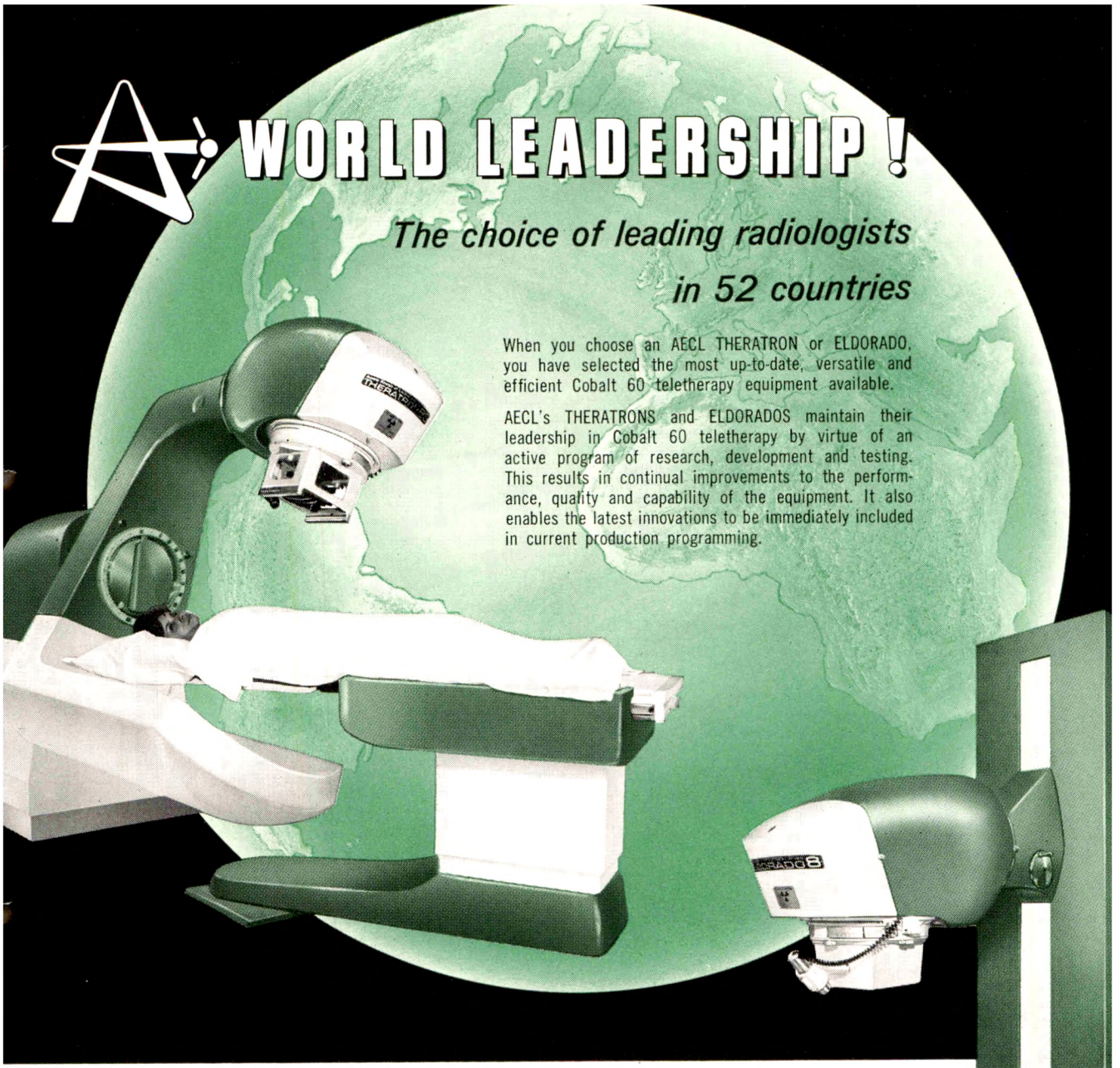
Mobile Fluoricon tracks either straight ahead or side-to-side. C-arm rotates 180° side-to-side, 90° front-to-back . . . travels 18-inches vertically.

All told, Mobile Fluoricon image intensifier delivers unmatched mobility and image presentation where and when you need it. Truly, information on the move.

Progress is our most important product

GENERAL ELECTRIC

MILWAUKEE, WISCONSIN 53201



The THERATRONS with their versatility, coupled with the flexibility of couch movement and positioning, all operated with finger tip control from a single, 15 ounce, hand held selector, provide the optimum in speed and ease of setup for the prescribed treatment.

The ELDORADOS, fixed beam teletherapy units, have a record of efficiency, economy and dependability that is unmatched by any other Cobalt 60 teletherapy equipment.

AECL's WORLD LEADERSHIP in Cobalt 60 teletherapy is the result of a long record of **proven performance.** World wide representation provides immediate service — anywhere! For detailed information please write to the address below.

Atomic Energy of Canada Limited
Commercial Products

68.3M

P.O. Box 93, Ottawa, Canada • Tel. 836-2790 • Area Code 613 • Cable 'NEMOTA'

INDEX TO ADVERTISERS

Abbott Laboratories ..... vi, vii, lxx, lxxi
AGA Corporation lxxxiv
Amersham/Searle Corporation ..... lxxxix, xci
Artronix, Incorporated li
Atomic Energy of Canada Ltd. xciii

Baird-Atomic, Inc. lxxxv
Barnes-Hind Barium Products ..... xxxviii, xxxix
Baruch Instruments Corporation xii
Buck X-Ograph Company lxxiv

Dunlee Corporation ..... xxxiv, xxxv
du Pont, E. I., de Nemours Co. ..... lii, liii

Eastman Kodak Company ..... xlvii, xlviii, xlix
Elema-Schonander, Inc. lxxxvi

Flow Pharmaceuticals, Inc. xc

GAF Corporation xxxiii
General Electric Company ..... x, xi, lviii, lix, xcii

Halsey X-Ray Products Company xxxvi
High Voltage Engineering i
Hunt, Philip A., Chemical Corporation ..... liv, lv

Ilford, Inc. xxxii
Isotopes l

Keleket X-Ray Corporation xcvi

Lafayette Pharmacal, Inc. xiii
Landauer, R. S., Jr. & Company xxxvii

Machlett Laboratories, Inc. ..... lxv, lxvi
Mallinckrodt/Nuclear Radiopharmaceuticals ..... lxviii, lxix
McElroy, Donald, Inc. li
3M Company (X-Ray Division) xx
Mosby, C. V., Company, The ..... lxxxvii, lxxxviii

Nuclear-Chicago Corporation ..... lxxii, lxxiii

Ohio-Nuclear, Inc. lxxviii
Ortho Pharmaceutical Corporation lxiv

Pako Corporation lxxv
Pharos Viewing Equipment Co. lxvii
Picker Nuclear Corporation ..... Second Cover, xiv
Picker X-Ray Corporation ..... lx, lxxix, Fourth Cover
Profexray, Inc. ..... lxxvi, lxxvii
Provincial Cancer Hospitals Board (Edmonton, Alberta, Canada) ..... lxvii, xcv
Purdue Frederick Company, The v

Schick X-Ray Company viii
Siemens Medical of America, Inc. xxxi
Squibb, E. R., & Sons, Inc. ..... xv, xvi, xvii, xli, xlii, xliii, lvii, lxi, lxii, lxiii, lxxx, lxxxi
Standard X-Ray Company lvi

Thomas, Charles C, Publisher ..... ix, xii, xcv

U. S. Veterans Administration Hospital (Augusta, Ga.) lxvii

Varian Radiation Division ..... lxxxii, lxxxiii

S. S. White Company xl
Winthrop Laboratories .....
....xviii, xix, xxi, xxii, xxiii, xxiv, xxv, xxvi, xxvii, xxviii, xxix, xxx, xliv, xlv, xlvi
Wolf X-Ray Corporation ..... Third Cover

•

We try to present an accurate index. Occasionally this may not be possible because of a last-minute change or an omission.

Director of Nuclear Medicine

Dr. W. W. Cross Cancer Institute

Edmonton, Alberta, Canada

Applications are invited for the position of Director of Nuclear Medicine at our new cancer hospital.

Edmonton is a rapidly growing city with excellent educational and recreational facilities—only 4 hours driving time from the Rocky Mountains.

On July 1, 1968 our new 78 bed Cancer Hospital was completed, containing extensive Radio Isotope, Diagnostic and Therapeutic Radiology and Medical Physics departments and other support facilities. The Radiotherapy Department includes two cobalt units, a cecium unit, deep and superficial x-ray units, and a linear accelerator to be installed in several months. Fully modern isotope facilities are available including a double headed rectilinear scanner with 8 inch crystals, gamma camera etc. and a new separate isotope laboratory. Case load of 2000 malignancies annually are referred through the new Cancer Hospital. There is also the opportunity for clinical research.

Effective January 1, 1969, the salary range is $22,000 to $27,000 per annum.

There is a superannuation scheme, relocation allowance, group life insurance and other fringe benefits.

Further information and application forms can be obtained from Dr. J. R. Ibberson, Executive Director, Provincial Cancer Hospitals Board, 11560 University Avenue, Edmonton, Alberta, Canada.



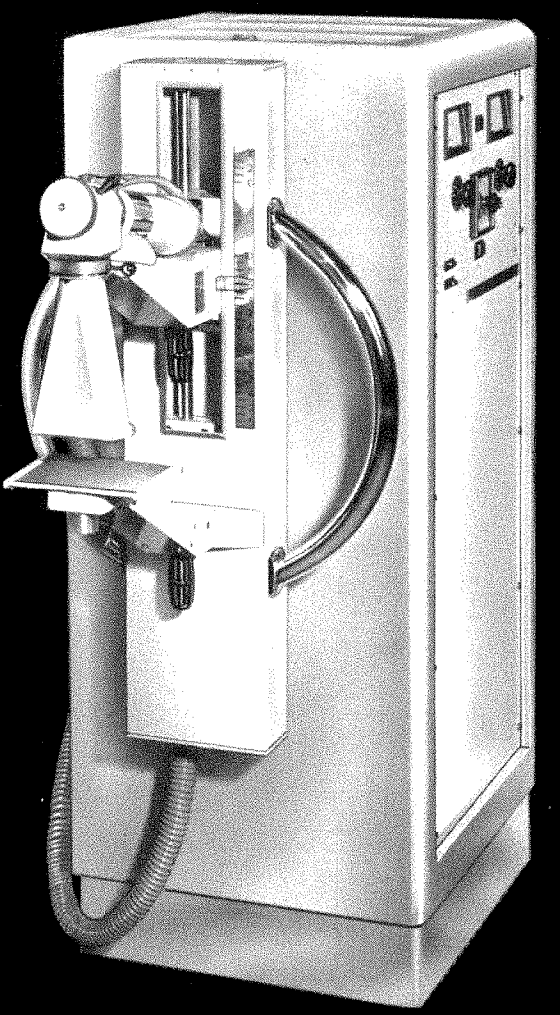
FOR THE RIGHT ANSWER WHEN YOU NEED IT . . .

- **MEDICAL RADIOGRAPHIC TECHNIC (3rd Ed., 2nd Ptg.).** *Rewritten by* **William L. Bloom, Jr., John L. Hollenbach,** and **James A. Morgan,** *all of the Technical Service X-Ray Dept., General Electric Company, Milwaukee.* '67, 368 pp. (7 × 10), 510 il., 7 tables, $11.00
- **A BIOLOGICAL CONSIDERATION OF TREATMENT OF BREAST CANCER** *by* **George Crile, Jr.,** *Cleveland Clinic, Ohio.* '67, 204 pp., 28 il., 17 tables, $8.00
- **CASE OF THE DAY** *by* **Benjamin Felson** *and* **Jerome F. Wiot,** *both of Univ. of Cincinnati, Ohio.* '67, 96 pp. (6¾ × 9¼), 91 il., $8.50
- **RADIOLOGY AS AN ART AND OTHER ESSAYS** *by* **John L. McClenahan,** *Hosp. of The Univ. of Pennsylvania, Philadelphia.* '67, 104 pp., 3 il., $5.75
- **ILLUSTRATIVE CRANIAL NEURORADIOLOGY** *by* **Alfred L. Schmitz,** *Univ. of California, Los Angeles;* **Samuel B. Haveson,** *Univ. of Southern California, Los Angeles; and* **Duke Hanna,** *Freeman Memorial Hosp., Inglewood.* '67, 404 pp. (8½ × 11), 532 il. (1 in full color), $31.50
- **ERROR AND VARIATION IN DIAGNOSTIC RADIOLOGY** *by* **Marcus J. Smith,** *St. Vincent Hosp., Santa Fe.* '67, 208 pp., 68 il., 18 tables, $8.75
- **TREATMENT FOR CHROMOPHOBE ADENOMA** *by* **Hendrik J. Svien** *and* **Malcolm Y. Colby, Jr.,** *both of Univ. of Minnesota, Rochester.* '67, 116 pp. (6¾ × 9¼), 60 il., 15 tables, $7.50
- **CLINICAL RADIOISOTOPE SCANNING** *by* **Yen Wang,** *Univ. of Pittsburgh, Pa.* '67, 260 pp. (6¾ × 9¼), 280 il., 8 tables, $12.50

CHARLES C THOMAS · PUBLISHER
301-327 East Lawrence Avenue
Springfield · Illinois · 62703

High Contrast of low density differences

in Mammography with the Senograph



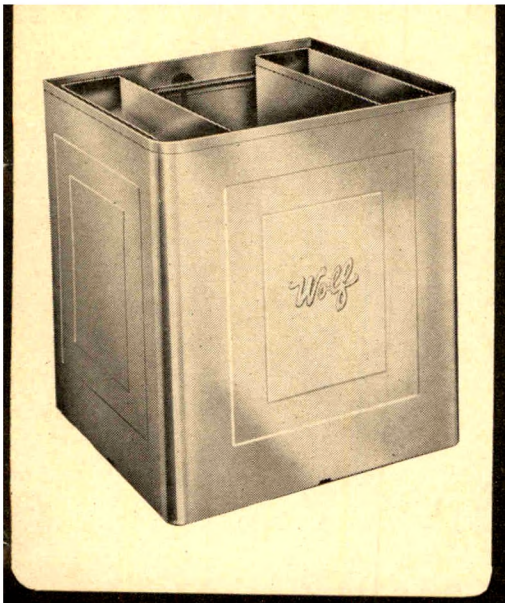
A new concept for specialized mammography examinations . . . now delivers better information faster.

Increased dynamic range pays off — in exceptional contrast enhancement by making slight opacities conspicuous — in diagnosis with a greater confidence factor.

More patients can be examined more thoroughly during any fixed time period — because of simplified and precise positioning capability, which encourages patient co-operation.

For Details — Contact Local Dealer or Write Us

KELEKET CGR





BRILLIANT DEVELOPMENT

The doctor's diagnosis and the well-being of his patient often depend upon the development of clear, sharp X-ray [illegible]ere margin for error, no room for second best... and so it must be the way with the equipment you use. Herein lies the importance of usin advanced, all-new WOLF Stainless Steel Developing Tank with remo inserts... precision engineered to be the finest of its kind in the worl signed to be the reliable workhorse today's advanced science of genology demands! When you're ready to order, just remember tha greatest x-ray technician, using the finest machine and film available, await, rely and act upon the results produced in his developing tank. "WOLF" has proven to be the name you can rely on, everytime!

For your free brochure with complete details, write your dealer or Wolf today.

WOLF X-RAY CORPORATION

NEW YORK • CHICAGO • LOS ANGELES • TORONTO

Executive Offices: 182-20 Liberty Avenue, Jamaica, New York 11412

WOLF X-RAY CORP. Wolf NEW YORK

Somewhere near you, a radiologist is getting the sharpest images he's ever seen because of this new table.

Hundreds of radiologists now working with the new Picker "Galaxy" table are getting the best images they've ever experienced: the sharpest fluoroscopy, spotfilms, and Bucky radiographs. And because their everyday practical experience is likely to be more revealing than our technical explanations, you might wish to seek out a current user of the "Galaxy" table. (If you need help with this search, let us know. We'll help you set up a visit.)

Until then, the following technical explanations can provide background as to why the "Galaxy" table produces such superb images.

The table is so structurally rigid that it thoroughly tames the subtle (and some not-so-subtle) vibrations all too often encountered in x-ray tables. The improvement in image sharpness resulting from such suppression is dramatic.

The "Galaxy" collimating system optimizes imaging geometry by significantly refining the relationship of focal spot, shutter plane, film plane, and patient plane. Geometric unsharpness and penumbra, for instance, are abated by locating the fluoroscopic shutter 30% farther from the focal spot than is customary.

Another important point about the "Galaxy" system is the way its automatic coning improves radiographic contrast, reduces scatter radiation, and minimizes dosage to patients and operators.

And now for help in finding a nearby "Galaxy" table user to speak to—or for more information from us—contact your local Picker representative or write Picker Corporation, 595 Miner Road, Cleveland, Ohio 44143.

PICKER



FOUNDED IN 1906 AS THE AMERICAN QUARTERLY OF ROENTGENOLOGY

THE AMERICAN JOURNAL OF ROENTGENOLOGY RADIUM THERAPY AND NUCLEAR MEDICINE

CALCUTTA MEDICAL COLLEGE LIBRARY UNIVERSITY

OFFICIAL ORGAN OF
THE AMERICAN ROENTGEN RAY SOCIETY
THE AMERICAN RADIUM SOCIETY

TRAIAN LEUCUTIA, Editor
KENNETH L. KRABBENHOFT, Assistant to the Editor

ASSOCIATE EDITORS
HARRY HAUSER RUSSELL H. MORGAN EDWARD B. D. NEUHAUSER

CONSULTING EDITORIAL BOARD
OSCAR V. BATSON
JOHN CAFFEY
ROSS GOLDEN
PAUL C. HODGES
HOWARD B. HUNT
JOHN H. LAWRENCE
REED M. NESBIT
EUGENE P. PENDERGRASS
LAURISTON S. TAYLOR
OWEN H. WANGENSTEEN
SHIELDS WARREN

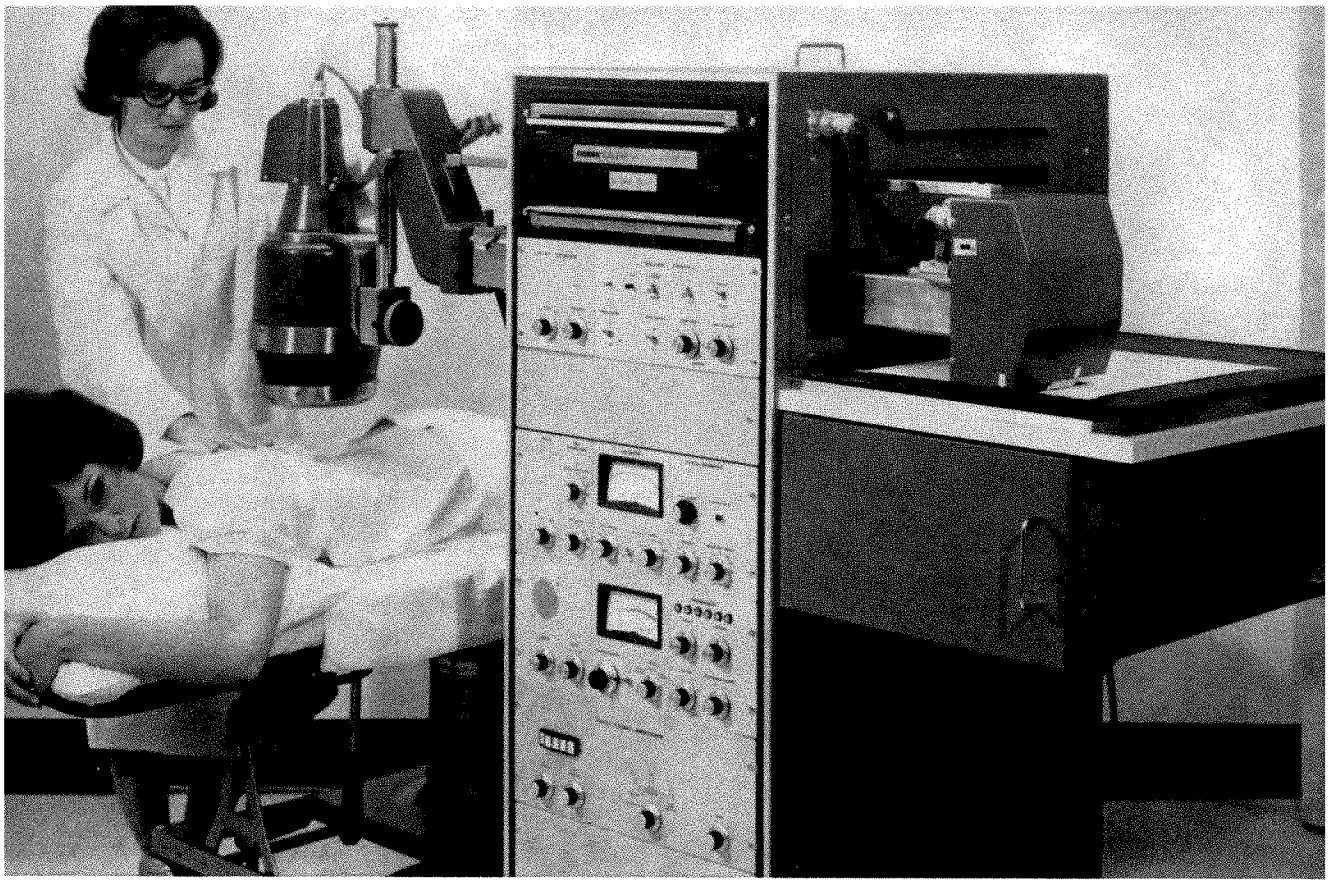
Issued Monthly for the American Roentgen Ray Society by
CHARLES C THOMAS · PUBLISHER · SPRINGFIELD · ILLINOIS · 62703

VOLUME 105 APRIL, 1969 NUMBER 4

Fifty-first Annual Meeting, American Radium Society
Bellevue Stratford Hotel, Philadelphia, Pennsylvania 19102
April 27-30, 1969

For Preliminary Program see January Issue

INDEX NUMBER



The case for the classical radioisotope scanner, or...

Why does Picker keep refining and improving its basic rectilinear scanner (Magnascanner® 500), when it also has a most sophisticated high-speed scanner (Dynapix®), and two exceptional cameras (Dynacamera™ and Magnacamera®)?

Because: despite the rapid forward thrust of progress —which we ourselves aid, abet, foster and contribute to —nothing we or anyone else has done has obsoleted the basic rectilinear scanner. What basic scanners do, nothing does better, and few do as well. Examples?

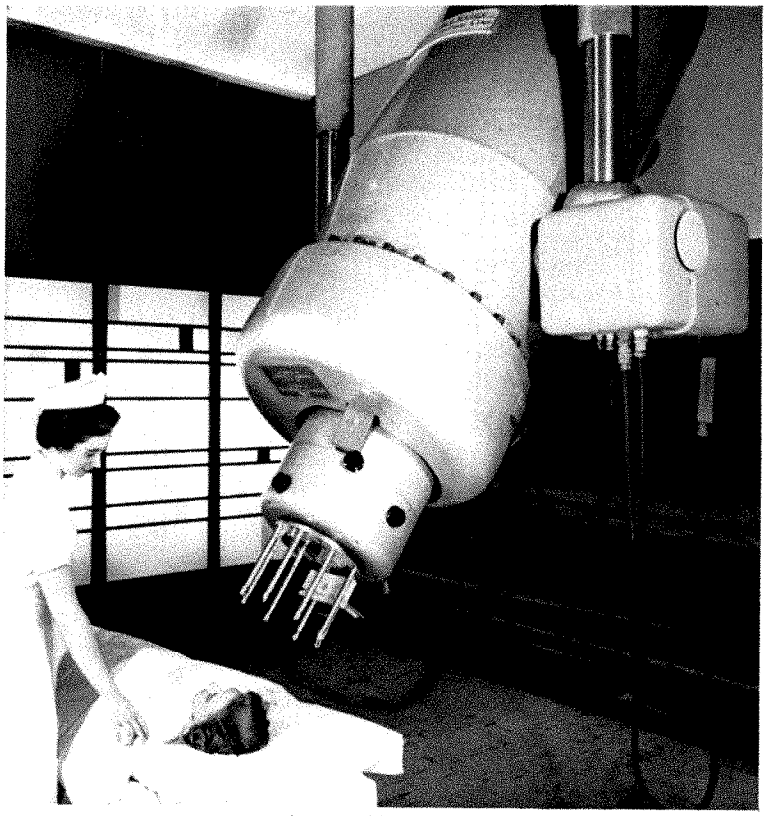
For a small hospital starting a diagnostic radioisotope laboratory with a small patient load and a modest budget, there is nothing quite as appropriate as a scanner. Hence, four out of five nuclear medicine departments get started with a Magnascanner and there are now over 2500 in use throughout the world. Similarily, a Magnascanner is a most relevant choice for larger hospitals in need of an instrument with the highest resolution for diagnostic confirmation. A basic scanner like the Magnascanner is still the best device available for static-imaging applications by virtue of its very high resolution, large field of view, wide energy range, contrast enhancement, wide choice of focusing collimators, and modest cost.

None of this should imply that the Magnascanner is an untouched island in the stream of progress. Today's instrument is generations away from yesterday's. Note: (1) maximum scan speed has been increased from 200 cm/min to 500 cm/min; (2) detector can be positioned by a control on the detector head itself, and a ratemeter on the detector head facilitates and speeds location of "hot" and "cold" spots; (3) a new color photo recording system is available in addition to black and white photorecording, multicolor dot recording, and Teledeltos black dot recording; (4) push button energy window selection (in addition to manual selection) for the most common radioisotopes used in diagnosis.

And Now the Dual Magnascanner®—This instrument is essentially identical to the Magnascanner® 500 except that it has two separate opposed detectors which acquire information independently. AP and PA, or RL and LL rectilinear scans can be performed simultaneously. This capability minimizes the need for patient re-positioning and reduces the scanning time by half.

Further information is available—Please write for detailed information on the Magnascanner® 500 and the Dual Magnascanner to Picker Nuclear, 1275 Mamaroneck Avenue, White Plains, N.Y. 10605. Please request file 235R.

PICKER

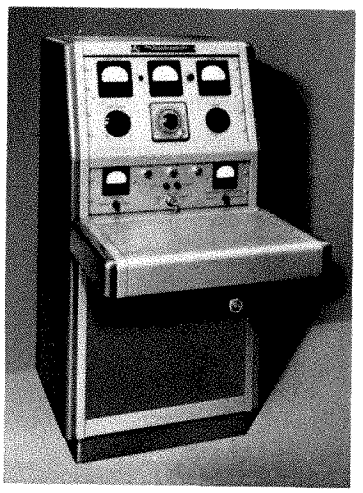


Improved Model AM Van de Graaff is the result of experience gained in 40 previous installations.

IMPROVED *Van de Graaff*® ACCELERATOR MEETS THE MODERN NEED FOR LOW-COST PRECISION THERAPY

Today's Model AM 2 MeV Van de Graaff Therapy Unit continues to keep pace with the trend to low-cost precision therapy in leading hospitals and cancer clinics throughout the Free World. And for five good reasons:

- Its less than 3 mm "point source" of x-rays allows optimum technics for both large and small treatment fields.
- Its treatment beam is accompanied by negligible penumbra.
- Its Roentgen output exceeds that of a 5000 curie cobalt source.
- Its x-ray output will not fall off. You can hold treatment techniques and parameters constant.
- It can be operated easily by a technician without a staff physicist in attendance.



The Model AM Van de Graaff is a reliable, proven source of high-energy radiation. It offers more roentgens-per-dollar and has demonstrated less overall cost-per-treatment than any other comparable supervoltage source available today — including radioisotopes.

Full time use of the reliable Model AM 2 MeV Van de Graaff Therapy Unit will amplify your technic range and expand your patient handling capacity. It is backed by the international reputation of the leading manufacturer of particle accelerators — High Voltage Engineering Corporation. Write Medical Sales.

Today's Model AM is routinely operated by an easily-trained technician.

HIGH VOLTAGE ENGINEERING CORPORATION
BURLINGTON, MASSACHUSETTS

Manuscripts offered for publication and other correspondence relating to the editorial management and books for review should be sent to Dr. Traian Leucutia, Editor, 401 Professional Building, Detroit, Michigan 48201. Contributions may be sent in foreign languages and will be translated if found acceptable. Original articles are published with the understanding that they are contributed exclusively to THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE.

A certain number of illustrations will be supplied free of cost; but special arrangements must be made with the Editor and Publisher for excess illustrations and elaborate tables.

Fifty reprints are furnished without charge to authors. Additional reprints may be purchased according to a scale of prices that accompanies galley proofs. As soon as each issue is printed, the type is destroyed except for reprint orders *in hand*. Reprint orders *must* be returned with corrected galley proof to the Editorial Office if additional reprints are desired.

Correspondence regarding subscriptions, advertisements, and other business relating to THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE should be addressed to Charles C Thomas, Publisher 301–327 East Lawrence Avenue, Springfield, Illinois 62703. (All requests to be submitted in writing.)

Manuscripts should be typewritten, with double spacing, and good margins (not on thin paper) and the *original* should be sent to the Editor. The author should keep a carbon copy, as the original is not returned. The name of the author should appear on each sheet of manuscript. Tabular materials should be typed on separate sheets; likewise bibliographical lists, footnotes, etc.

Drawings and charts for reproduction should be made in black (*never* in blue). Photographic prints of plates or slides on glossy paper produce the best half-tones.

All photographs and drawings intended for illustrations should be numbered, the top plainly indicated, and an abbreviated title of the paper placed on the back of *each one.*

Legends for illustrations should be typewritten in a single list, double spaced, with numbers corresponding to those on the photographs and drawings, instead of attaching each legend to its corresponding figure.

Care in preparation of bibliographies will save much time and correspondence. Each reference in a bibliography should include the following information in the order indicated: Name of the author with initials; title of the article; name of the periodical; year, volume and pages. It is requested that the authors use the following as model:

1. Olcott, C. T., and Dooley, S. W. Agenesis of lung of infant. *Am. J. Dis. Child.*, 1943, *65*, 766–780.

The month should be given if the reference is to an issue of the current year. An alphabetical arrangement of the authors is requested.

The author should always place his full address somewhere on his manuscript. This is very important and is often omitted.

For information regarding membership in the American Roentgen Ray Society, address the Chairman of the Executive Council, Dr. E. F. Van Epps, Duke University, Durham, North Carolina 27706.

For information regarding the program of the annual meeting of the American Roentgen Ray Society, address the President-Elect, Dr. James C. Cook, LL 14 Professional Plaza, 3790 Woodward Avenue, Detroit, Michigan 48201.

For information regarding membership in the American Radium Society, address the Secretary, Dr. John V. Blady, The Parkway House, 2201 Benjamin Franklin Parkway, Philadelphia, Pennsylvania 19130.

For information regarding the program of the annual meeting of the American Radium Society, address the President, Dr. Juan A. del Regato, Penrose Cancer Hospital, 2215 North Cascade Avenue, Colorado Springs, Colorado 80907.

THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE is owned, maintained by, and in the interests of the American Roentgen Ray Society, Inc. It is issued monthly by Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Illinois 62703. THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE does not hold itself responsible for any statements made or opinions expressed by any contributors in any article published in its columns.

Delivery is not guaranteed. Replacements are not guaranteed nor promised, but will be attempted if extra single copies are available and only if requested within 30 days from first of month following publication (17th of month) for domestic subscribers and 60 days for foreign subscribers.

Annual subscription price is as follows: United States, U. S. Possessions, U. S. Trusteeships, Pan-American Union, and Canada, $20.00; other countries $22.00. Prices for back volumes quoted on application. Extra single copies of back issues, if available, $2.00, postpaid. Current subscriptions may begin with any issue. Remittance should be sent to CHARLES C THOMAS, PUBLISHER, 301–327 East Lawrence Avenue, Springfield, Illinois 62703, U.S.A.

ADDRESS CHANGE—When a change of address is necessary please allow at least 60 days notice and preferably 90 days. When ordering a change of address, send the Publisher both the old and new address.

Entered as Second-class at Springfield, Illinois under the Act of March 3, 1879. Printed in U.S.A.
Second-class postage paid at Springfield, Illinois and at additional mailing offices.

Copyright © 1969, by AMERICAN ROENTGEN RAY SOCIETY, Inc. No part may be duplicated or reproduced without permission of both the Publisher and the Editor.

THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE

VOL. 105 APRIL, 1969 NO. 4

TABLE OF CONTENTS

Fluorescent Thyroid Scanning. PAUL B. HOFFER, M.D. 721

Serial Brain Scanning with Technetium 99m Pertechnetate in Cerebral Infarction. MICHAEL S. USHER, M.D., AND JAMES L. QUINN, III, M.D. . . 728

Radiation Response in Relation to the Cell Cycle In Vivo. JACOB I. FABRIKANT 734

Patterns of Protein Synthesis in the HeLa Cancer Cell. GERALD M. KOLODNY, M.D. 746

Roentgenologic Studies of Cerebrospinal Fluid Formation in the Dog. D. GORDON POTTS, M.D., AND RICHARD M. BERGLAND, M.D. . . 756

Lipid Embolism to the Brain Following Lymphography; Case Report and Experimental Study. J. W. DAVIDSON, M.B. 763

Contrast-Vasoconstrictor Mixtures in Angiography. PAUL C. KAHN, M.D., with the technical assistance of JOSEPH P. ZEPPIERI, A.B., AND GERALD S. LORCH, B.S. 772

Effect of Angiocardiography on Fluid and Electrolyte Balance. AARON R. LEVIN, M.R.C.P. (Edin.), HERMAN GROSSMAN, M.D., EDWARD T. SCHUBERT, PH.D., PATRICIA WINCHESTER, M.D., AND ANGELA GILLADOGA, M.D. 777

Coronary Arteriography in Hypercholesterolemic Patients. HAROLD A. BALTAXE, M.D., KURT AMPLATZ, M.D., RICHARD L. VARCO, M.D., AND HENRY BUCHWALD, M.D. 784

Effects of Ionizing Radiation upon the Immature Rabbit Larynx. FREDERICK J. BONTE, M.D., VERNIE L. STEMBRIDGE, M.D., AND JAMES D. REEF, M.D. 791

Vascular Structure of Glioblastomas. J. H. SCATLIFF, M.D., W. B. RADCLIFFE, M.D., H. H. PITTMAN, B.S., AND C. H. PARK, M.D. . . . 795

The Basis for Segmental Sequential Irradiation in Hodgkin's Disease: Extended vs. Local Fields in the Radiocurability of the SJL/J Mouse Hodgkin's-Like Reticulum Cell Sarcoma. PHILIP RUBIN AND GLENN HALUSKA, with the technical assistance of GEORGE MILLER 806

The Basis for Segmental Sequential Irradiation in Hodgkin's Disease: Clinical Experience of Patterns of Recurrence. P. RUBIN, G. HALUSKA AND C. A. POULTER 814

(Continued on page iv)

The Lamina Dura (L. D.) of the Maxillary Antrum: Its Value in Roentgen Diagnosis. T. EL GAMMAL, M.B., AND THEODORE E. KEATS, M.D. 830
Tomography of the Temporal Bone in Paget's Disease. JERRY P. PETASNICK, M.D. 838
The Supracondylar Process and Its Fracture. ALEX NEWMAN, M.D. . . . 844
Triangular Cartilage Calcification in the Wrists: Its Incidence in Elderly Persons. WYLIE J. DODDS, M.D., AND HOWARD L. STEINBACH, M.D. . 850
A Study of Inter- and Intra-Observer Error in Reading Plain Roentgenograms of the Hands; "To Err is Human." JOHN H. BLAND, M.D., A. BRADLEY SOULE, M.D., FREDERICK W. VANBUSKIRK, M.D., ESTELLE BROWN, B.S., AND RUTH V. CLAYTON 853
Epiphyseal Dysostosis. HOWARD L. STEINBACH, M.D., AND ROBERT A. BROWN, M.D. 860
Use of a Digital Computer in the Measurement of Roentgenographic Bone Density. FRED B. VOGT, M.D., LOUIS S. MEHARG, PH.D., AND PAULINE BEERY MACK, PH.D. 870
Congenital Arteriovenous Malformation of the Foot. L. E. KELLERHOUSE, M.D., AND K. RANNIGER, M.D. 877
Mammographic Technique: Need for Routine Spot Roentgenograms. M. B. HERMEL, M.D., J. GERSHON-COHEN, M.D., AND R. N. BYRNE, M.D. 880
The Use of Hysterography in the Detection of Hydatidiform Mole. EDWARD I. GREENBAUM, M.D., G. PODOLAK, M.D., AND B. J. O'LOUGHLIN, PH.D. 885
A Roentgenologic Rule and Pelvimetry Technique. T. H. JOHNSON, JR., M.D., AND T. A. REAGAN, R.T. 890
Recovery of Detached Intravascular Catheter or Guide Wire Fragments; A Proposed Method. JOSEPH L. CURRY, M.D. 894
Skin Exposure from Handling Syringes Containing Radioactive Isotopes. R. S. CLAYTON, M.D., J. E. WHITE, M.D., M. BRIEDEN AND A. RODRIGUEZ, R.T. 897
The Independent Radiation Monitor (I.R.M.). PAUL M. KROENING, M.D., AND RAYMOND MUCHA 900
Three Dimensional Roentgenography. J. B. GARRISON, D. G. GRANT, W. H. GUIER, AND R. J. JOHNS 903
The Line Spread-Function and the Modulation Transfer Function of X-Ray Fluorescent Screen-Film Systems—Problems with Double-Coated Films. G. LUBBERTS, M.S. 909
Officers 918
Editorials
Winds of Change Pass Over the A.U.R. STANLEY M. ROGOFF, M.D. . 919
Palmer E. Wigby, M.D., 1903–1968. CURTIS H. BURGE, M.D. . . 921
News Items 922
Books Received 924
Society Proceedings 925
Abstracts of Radiological Literature 931
Subject Index to Volume 105 938
Author Index to Volume 105 949

"prep" the colon with pleasant-tasting X-PREP Liquid

(standardized extract of senna fruit)

Specifically designed for preradiographic bowel evacuation, X-PREP Liquid permits excellent visualization in G.I. and urologic roentgenography.

No significant gas shadows. No residual oil droplets.

X-PREP Liquid reduces or eliminates the need for enemas prior to radiography.

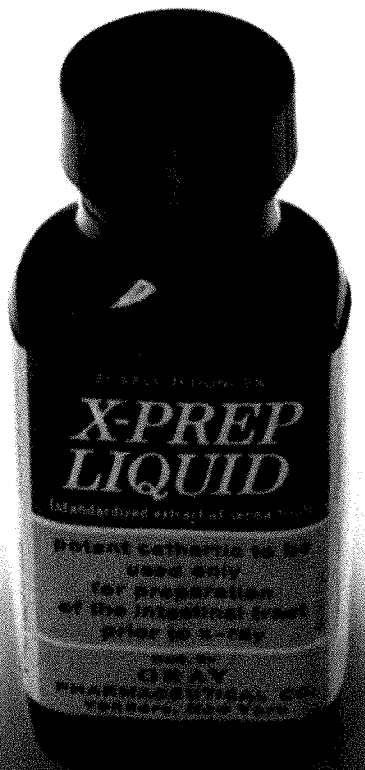
And delicious X-PREP Liquid gives a welcome reprieve for your patients from the obnoxious taste of castor oil.

Easy-to-take, X-PREP Liquid is also easy to administer. Premixed and premeasured, this effective bowel evacuant comes in small, single-dose bottles—to be taken between 2 and 4 p.m. on the day prior to radiography. Patients should be advised to expect strong purgative action.

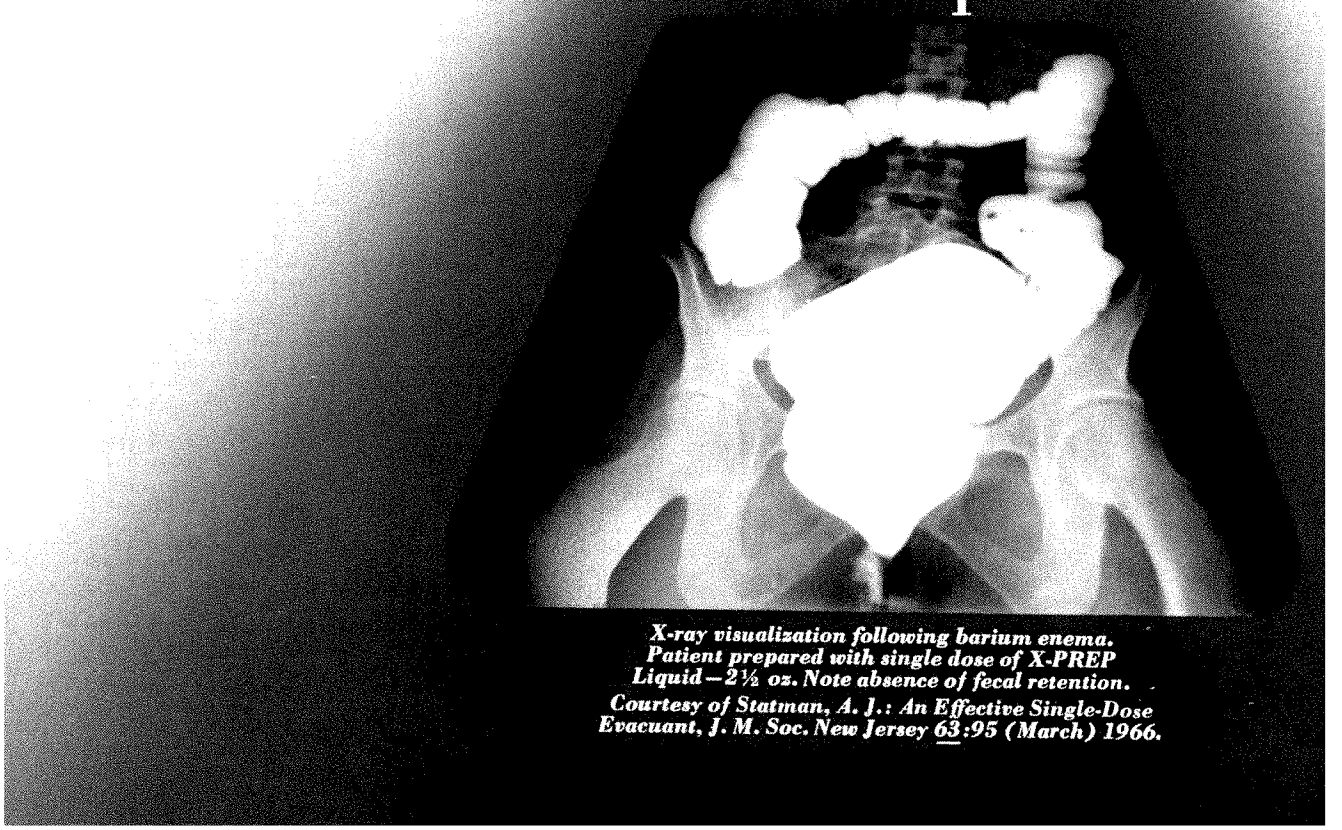
Contraindication: Acute surgical abdomen.
Supplied: Ready-to-drink in 2½ oz. bottles (complete adult dose).
Also available: X-PREP Powder (standardized senna concentrate). Mixed with water, ¾ oz. canister provides complete adult dose.

GRAY PHARMACEUTICAL CO., AFFILIATE,
THE PURDUE FREDERICK COMPANY,
Yonkers, New York

© COPYRIGHT 1968, GRAY PHARMACEUTICAL CO. E-23166R



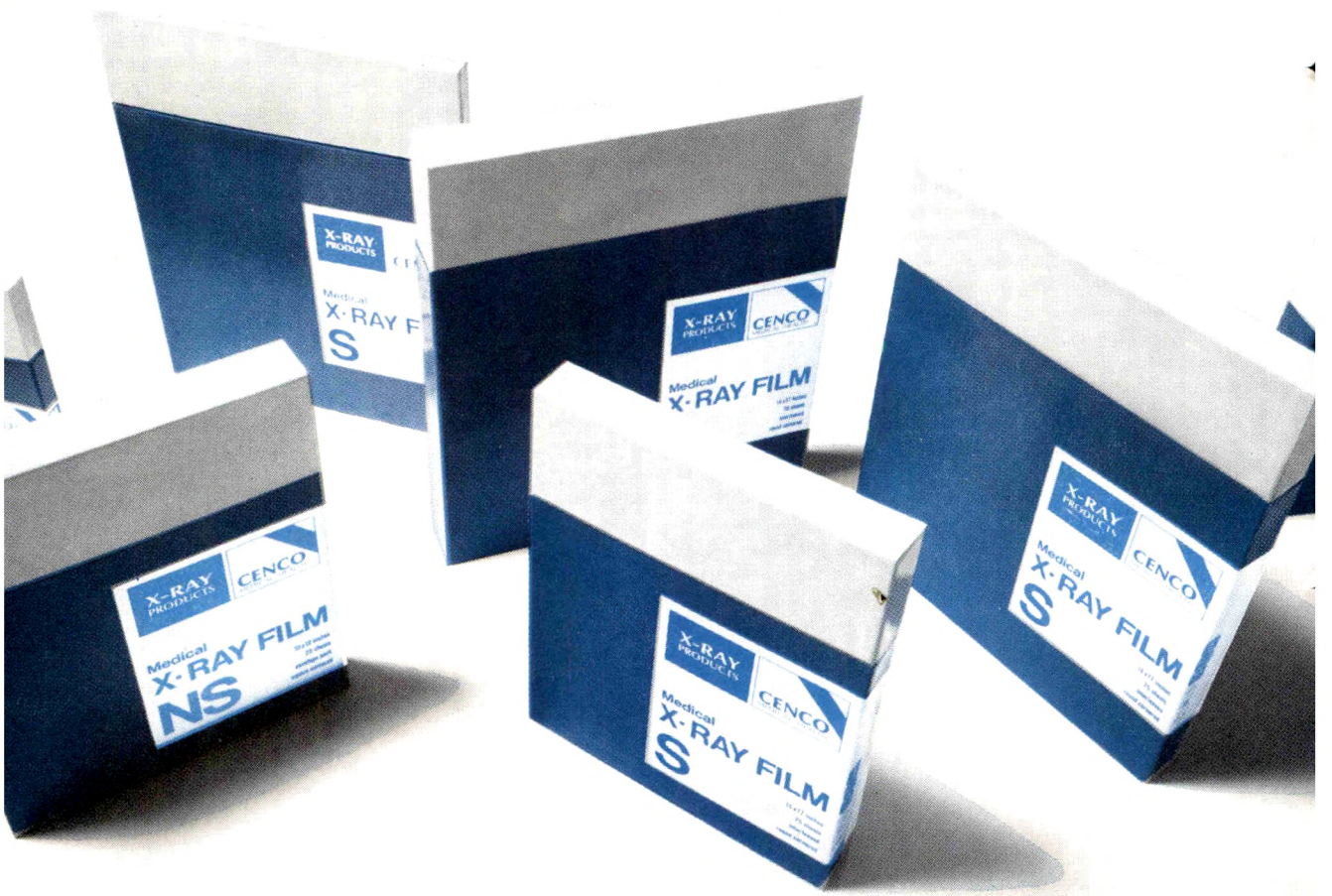
for a clear picture



X-ray visualization following barium enema. Patient prepared with single dose of X-PREP Liquid—2½ oz. Note absence of fecal retention.
Courtesy of Statman, A. J.: An Effective Single-Dose Evacuant, J. M. Soc. New Jersey 63:95 (March) 1966.

Cenco's great new line of medical x-ray film costs less than what you're probably using—and ours is just as good.

Which means it's better.



Actually in most instances, Cenco's medical x-ray film is better, *period*. Detail, definition, exposure latitude, and ultimate density are as good as the state-of-the-art of film manufacturing permits.

Just as important, Cenco's premium-quality film will work in any processing system—from hand tanks to 90-second automatic processors—or even in 60-second systems which are on their way.

Cenco Medical/Health: an important new factor in all phases of the hospital system. You'll be hearing soon from your local Cenco representative about these fine new films—and the processing chemistry that goes with them.

X-RAY PRODUCTS CENCO MEDICAL/HEALTH

CENCO MEDICAL/HEALTH, A SUBSIDIARY OF CENCO INSTRUMENTS CORP., 4401 W. 26TH ST., CHICAGO, ILL. 60623

Chicago, Ill. (312) 277-8300; Santa Clara, Calif. (408) 244-0212; Los Angeles, Calif. (213) 627-2533;
New York, N.Y. (212) GR 9-5900; Norfolk, Va. (703) 627-2506; Miami, Fla. (305) 642-6181.

Who took film processing out of the dark ages?



We did.

With the first really flexible film processor that works in daylight as well as dark.

It's self threading. Needs no leader with most films. You can feed it any size film—from 16 mm to 105 mm (a full 5 inches wide). In pieces as short as 5 inches long. At random. Interchangeably.

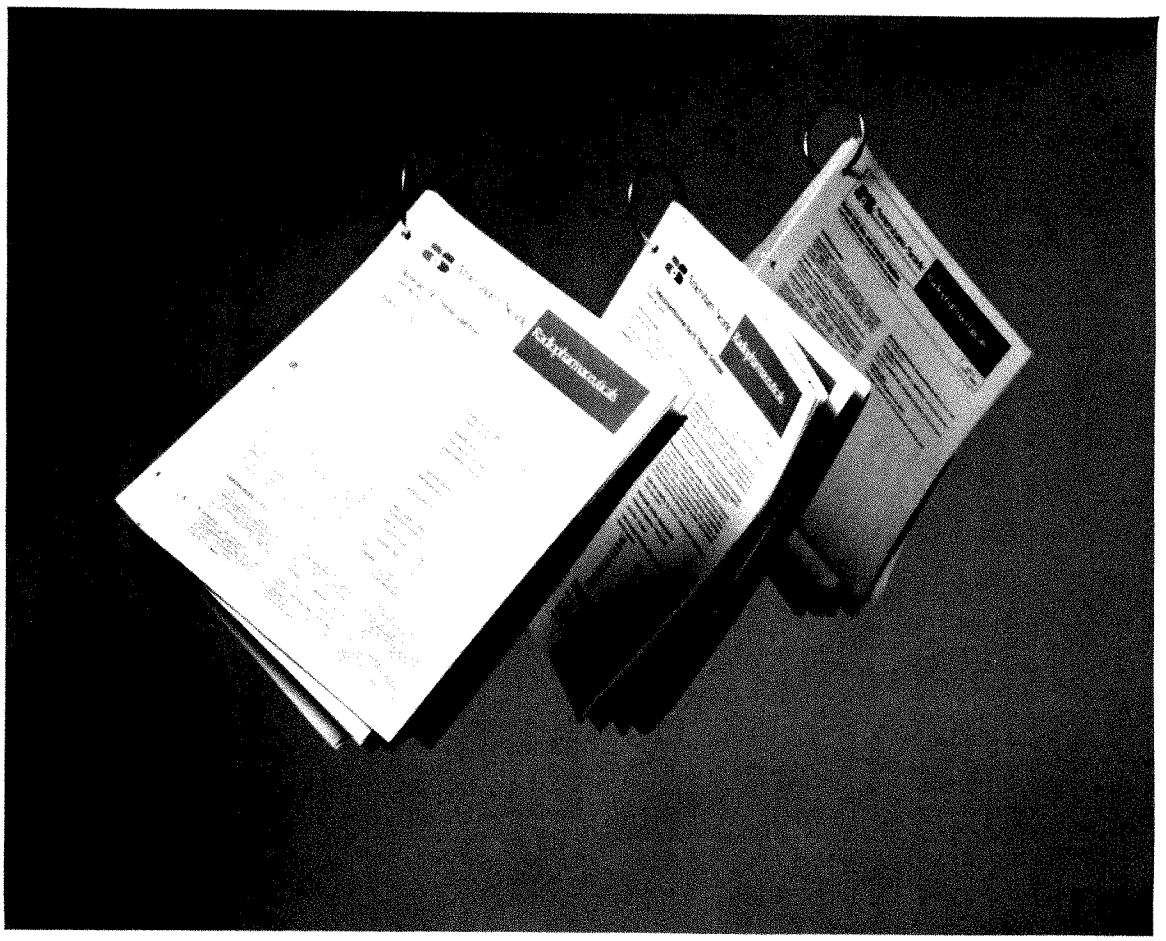
And that's not all. New, ingenious cassette design makes loading a cinch. Built-in controls deliver consistent results, no matter who the operator. And a simple water flush is absolutely the only daily maintenance the unit needs.

We'll be glad to show you how this award-winning, table-top processor fits into any nook, freeing some of your darkroom space for more productive use. Phone your local x-ray dealer or write direct.

Let us bring a little light into your life.

Automatic Seriograph Division
Litton Medical Products Group, Litton Industries
515 East Touhy Avenue • Des Plaines, Illinois 60018 • Telephone: (312) 296-4488

Think of them as a loose-leaf radiopharmacopoeia.



Our radiopharmaceutical bulletins. Detailed, invaluable clinical, biochemical, and chemical information on the wide variety of diagnostic compounds now offered by Amersham/Searle Corporation.

How wide a variety? Virtually everything from arsenic-74 to xenon-133—and building. Imaging agents for in-vivo techniques involving scanners and scintillation cameras. Labelled compounds for in-vitro metabolic studies. All available now from Amersham/Searle.

And whether it's information you get from us in print or in person, it comes from a knowledgeable source. Amersham/Searle was formed through a joint venture of The Radiochemical Centre, Amersham, England, and G. D. Searle & Co.

We therefore share in the technical excellence of The Centre in research, development, and manufacture of radiopharmaceuticals. Equally important as a resource is G. D. Searle, long a first-ranked name in pharmaceutical research and manufacture. Finally, we draw on the resources of Nuclear-Chicago Corporation (a Searle subsidiary)—a leading manufacturer of nuclear instrumentation.

So you see, we are in business to serve you as your primary source for radiopharmaceutical information and supply. For supplies and accessories for nuclear medicine.

Copies of our radiopharmaceutical bulletins are yours for the asking. As is our immediate, personalized attention to your needs. Write or call. B-219

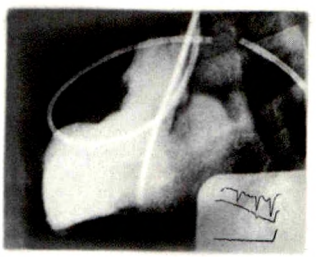
2000 NUCLEAR DRIVE DES PLAINES, ILLINOIS 60018 TELEPHONE: (312) 296-1055

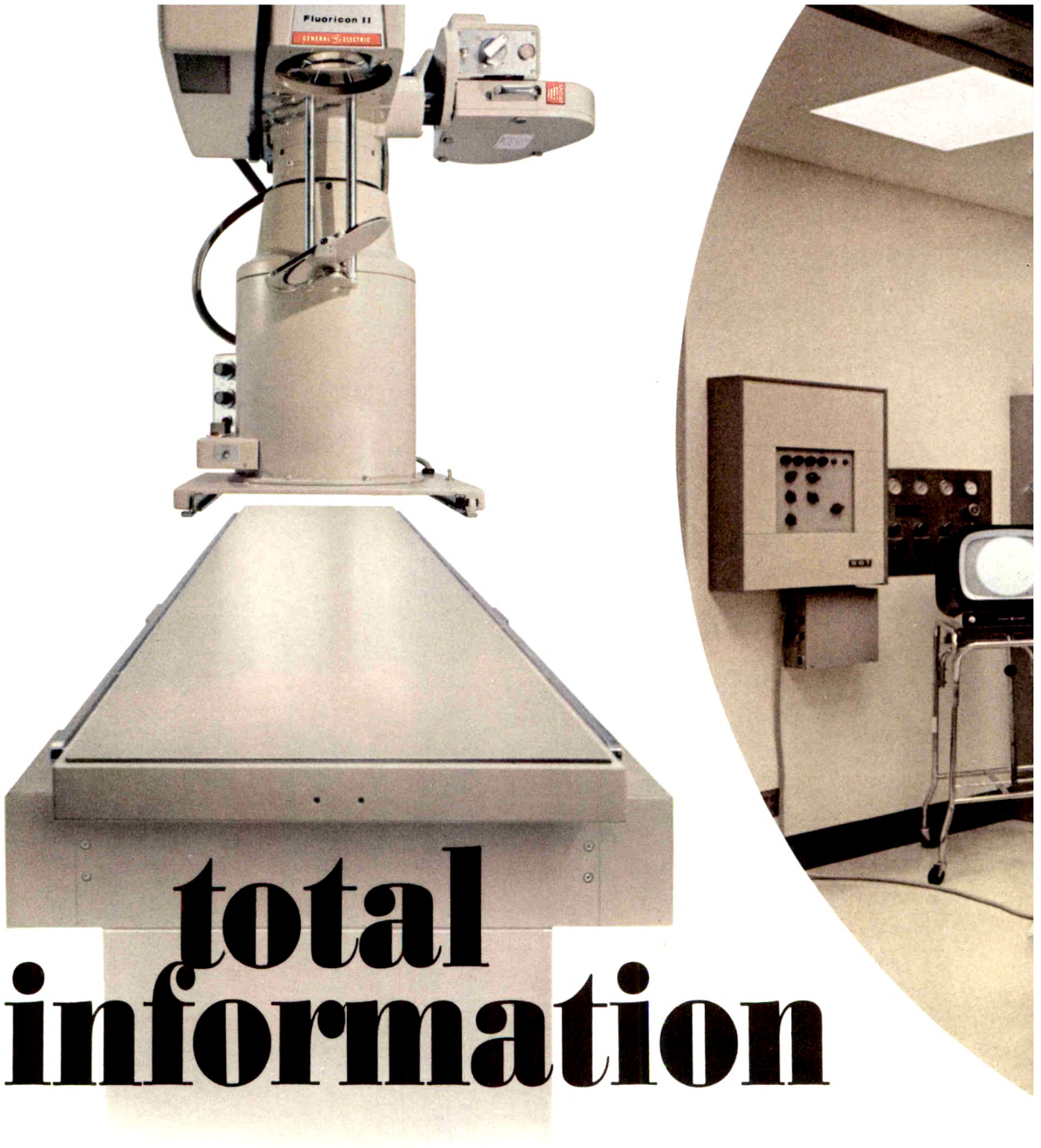
Amersham/Searle

AMERSHAM/SEARLE CORPORATION
AN ACTIVITY OF G. D. SEARLE & CO. AND THE RADIOCHEMICAL CENTRE



data for decision...





total information

More precise, more readily available, than with any other medical system. And Fluoricon® II image intensification makes the difference.

Information. Getting all you need is your concern. Our responsibility. Information: Accurate. Easy to correlate. Sharp presentation. Anatomical and physiological information displayed as one image. Everything that's needed to make demanding diagnostic decisions. Complete in one package.

Only GE Fluoricon II image intensification, with exclusive CFPD (Cine Fluoro Physiological Display), delivers all this . . . provides the unmatched "information heartbeat" for vascular procedures systems. Dual field image intensification, with television presentation, allows maximum coverage in normal mode and peak resolution in magnified mode. Choose 16 or 35 mm cine, or phototimed 70 mm spot film camera with patient identification. Brightness is controlled automatically to present the sharpest image possible at all times.



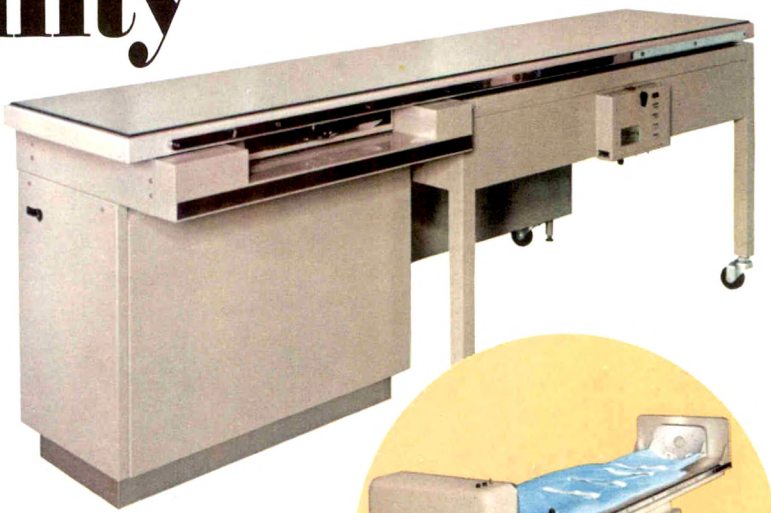
are recorded on cine film and displayed simultaneously on a TV monitor, and/or recorded on videotape. This filmed information is clear, accurate and precise. It presents your choice of from one to four channels of data — such as ECG, pressure(s), phonocardiograms and injection or other timed sequence sensitive data — in the combinations needed. CFPD facilitates the correlated cine study of both the physiological data and the actual anatomical image. Only GE offers this total information extra!

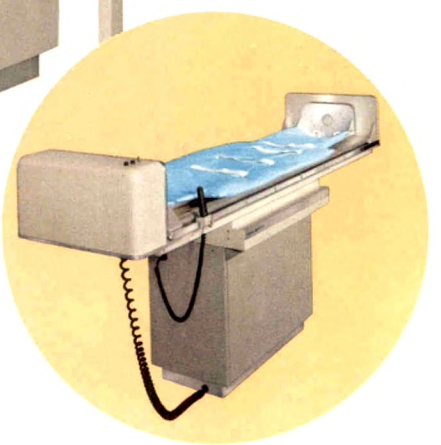
Whether it's for cardiovascular angiography, coronary arteriography, carotid/cerebral arteriography, abdominal arteriography, or cardiac catheterization and peripheral arteriography . . . GE Total Information Systems, with Fluoricon II image intensification, consistently deliver the critical information needed to make critical

MEDICAL SYSTEMS

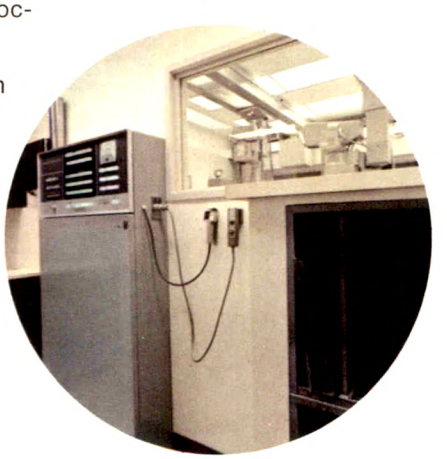
extended capability







New Model 75 catheterization table. Choice of tops: flat or rotating cradle. Top travels 55 inches longitudinally, permitting full use of rapid film changer and RIL seriograph; travels 10 inches laterally, 9 inches with Bucky. A push button on the control handle activates travel. Table height is adjustable at installation, 31-35 inches. A narrow 17 x 36 inch base allows doctor to work closer to patient without bending.



DXR-1250 3 phase, 12 pulse generator powers the system, with consistent linear output at all settings. Assures the power needed (i.e. 120 mAs in 1/10 of a second) for optimum contrast in rapid film changer applications.

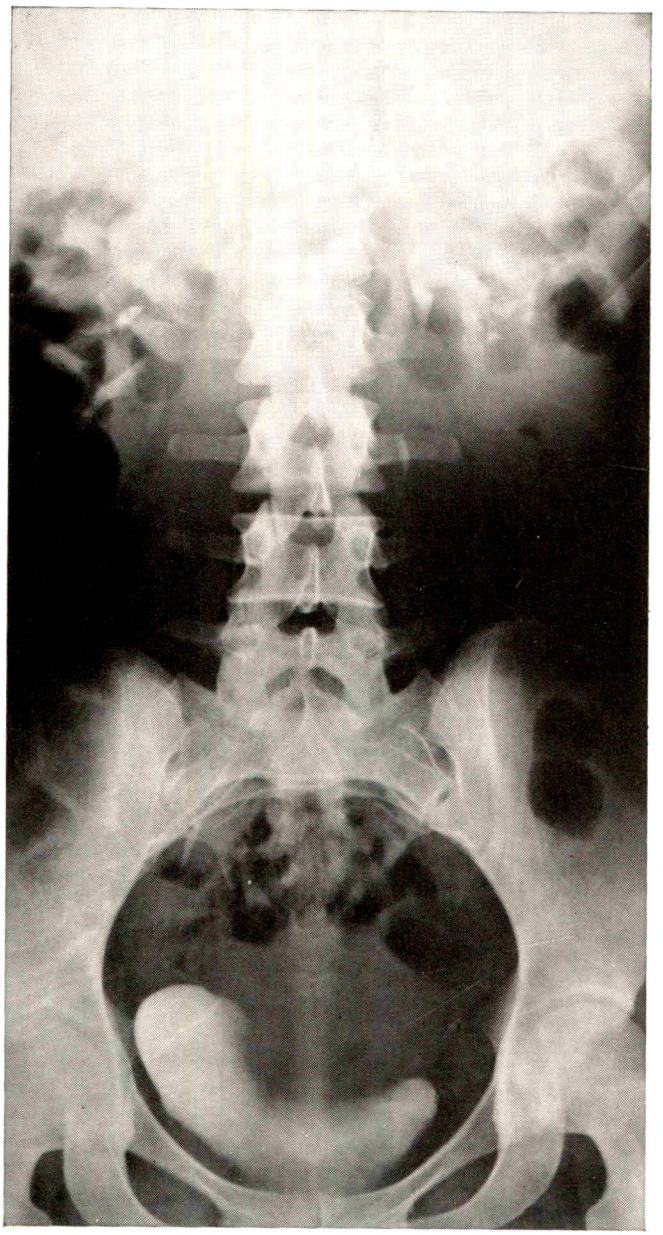
Ask about Maxiservice®, the full-service leasing and maintenance plan that lets you get the equipment you need now, with payments you can afford out of normal operating funds. Includes periodic service by GE technicians. Result: You're always sure of a smooth-operating system . . . to keep the vital information coming continuously.

Progress is our most important product

GENERAL ELECTRIC

MILWAUKEE, WISCONSIN 53201

Now!



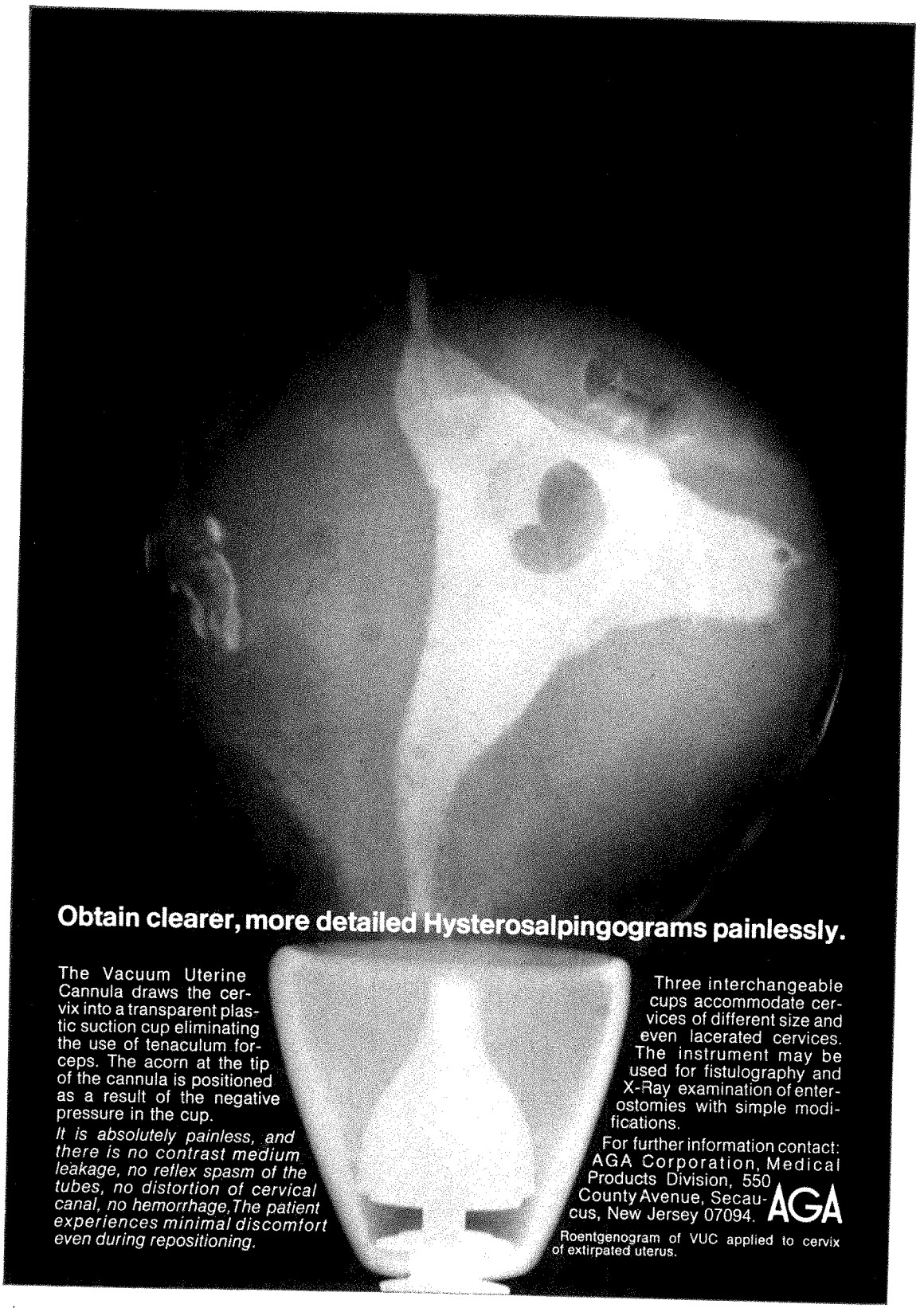
90 second Fuji film type Rx polyester base

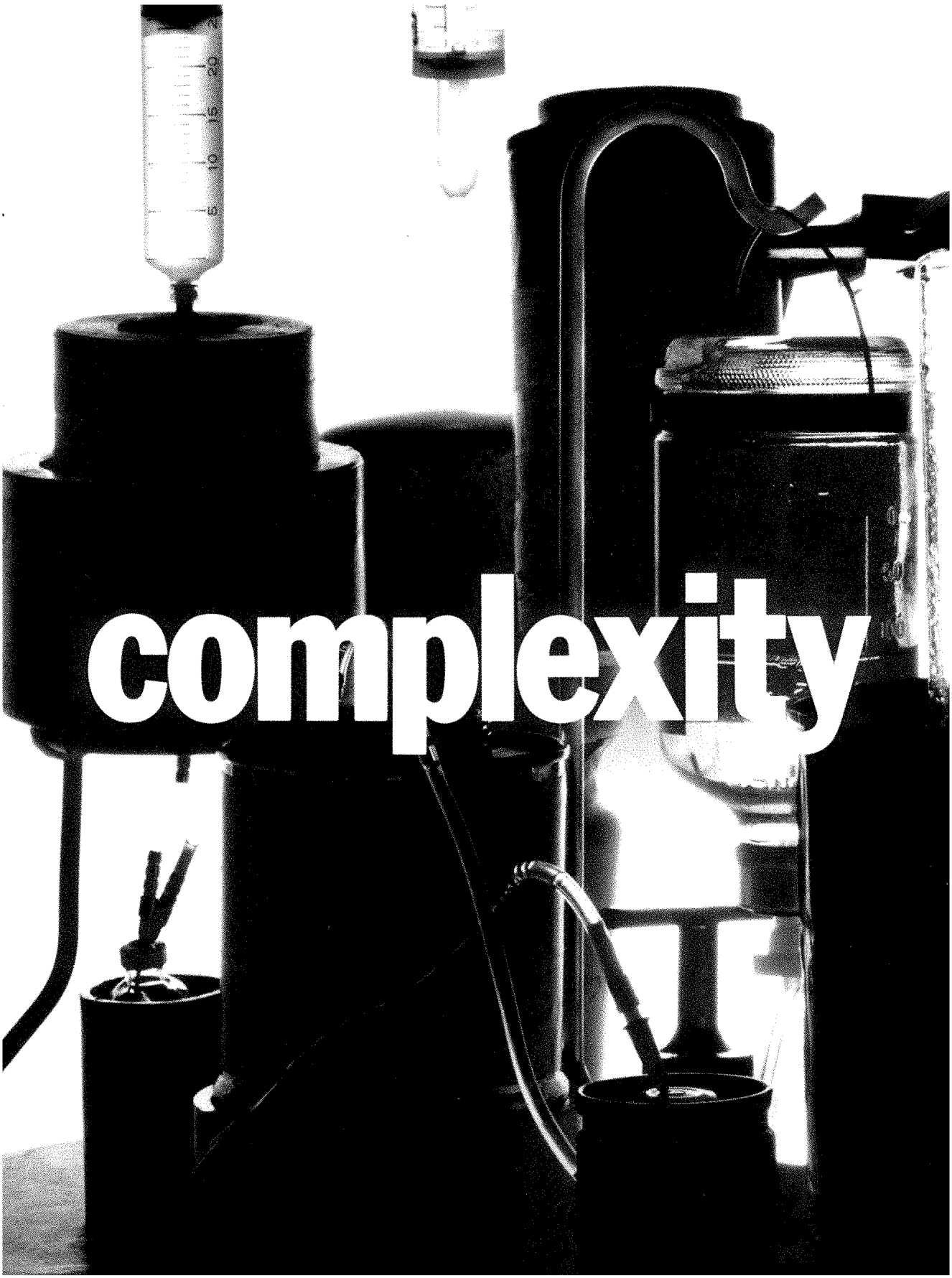
Available through
Pyne X-Ray and
their distributors

FUJI FILM

PYNE X-RAY CORPORATION

U. S. Distributors of FUJI Kx and Rx Film warehoused in New York, Chicago, Los Angeles
Dealers in all cities throughout the country.


Obtain clearer, more detailed Hysterosalpingograms painlessly.
The Vacuum Uterine Cannula draws the cervix into a transparent plastic suction cup eliminating the use of tenaculum forceps. The acorn at the tip of the cannula is positioned as a result of the negative pressure in the cup.
It is absolutely painless, and there is no contrast medium leakage, no reflex spasm of the tubes, no distortion of cervical canal, no hemorrhage.The patient experiences minimal discomfort even during repositioning.
Three interchangeable cups accommodate cervices of different size and even lacerated cervices. The instrument may be used for fistulography and X-Ray examination of enterostomies with simple modifications.
For further information contact: AGA Corporation, Medical Products Division, 550 County Avenue, Secaucus, New Jersey 07094.
AGA
Roentgenogram of VUC applied to cervix of extirpated uterus.


complexity


simplicity!
TECHNETOPE II
SQUIBB
CAUTION
RADIOACTIVE MATERIAL

SQUIBB
a research concept in nuclear medicine

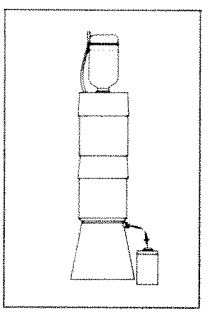
Introducing new Technetope® II

Squibb Technetium 99m STERILE GENERATOR

A FAR SIMPLER GENERATOR . . .
Hooks, hangers, and handles complicate assembly, so you won't find any on Technetope II. It's so simple that, after the usual aseptic techniques, assembly consists basically of two insertions into the generator column. Then attach an eluent bottle, an evacuated collecting vial, and milk. *That's* simplicity.

. . . DESIGNED WITH "T.D.S." IN MIND
Time: Technetope II simplicity reduces assembly time...keeping radiation exposure to a minimum. However, proper radiation safety precautions should be maintained at all times.
Distance: Technetope II allows you to keep your distance. You don't have to be constantly near the generator because it is self-milking. And eluate collection is made *at the side* of the unit—*away* from an unshielded port.
Shielding: Technetope II has another half-value layer of lead shielding—without adding a cumbersome dispenser, additional cost, or special contract.

In addition, Technetope II is readily adaptable to tandem milking which provides high concentrations of ^{99m}Tc per ml.—another Squibb first and exclusive.



Technetope II (Squibb Technetium 99m) Sterile Generator provides a means of obtaining a sterile, non-pyrogenic supply of Technetium 99m (^{99m}Tc). ^{99m}Tc, the short-lived daughter ($T_{1/2} = 6$ hours) of Molybdenum 99 (^{99}Mo, $T_{1/2} = 67$ hours), is obtained from the generator by periodic elution. The amount (in millicuries) of ^{99m}Tc obtained in the initial elution will depend on the original potency of the generator, while the activity obtained from subsequent elutions will depend on the time interval between elutions.

Warning: Proper radiation safety precautions should be maintained at all times. The column containing ^{99}Mo need not be removed from the lead shield at any time. The radiation field surrounding an unshielded column is quite high. Solutions of ^{99m}Tc withdrawn from the generator should always be adequately shielded. The early elutions from the generator are highly radioactive. For radiation protection, a lead shield for the collecting vial is included with Technetope II.

For additional information on this advanced generator or the tandem milking technique, please use the coupon below.

I would like to receive full information on:

☐ **Technetope® II** (Squibb Technetium 99m) Sterile Generator

☐ Tandem Milking with Technetope II

Please attach this coupon to your letterhead and mail to Medotopes Customer Service Dept., P.O. Box #7, East Brunswick, N. J. 08816.

Medotopes®

Squibb Division of Nuclear Medicine
East Brunswick, New Jersey 08816

Winning an award was not the object of Clinac® 4's grand design.



Photographed at Tumor Center, O'Connor Hospital, San Jose, California

A simple, reliable, high-output treatment system was.

The Clinac 4 linear accelerator was conceived to be the most advanced deep radiotherapy system of our time. As an operational reality, it now is fulfilling this promise. With an output of 350 Rads/min. in field sizes up to 32x32 cm. Providing the uniform high intensity that enables "mantle" treatments to be completed with ease in 2 to 3 minutes.

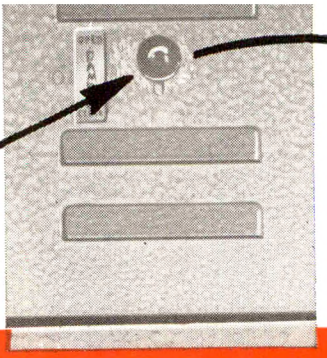
We thank the judging panel of WESCON for their award. If it now serves to spotlight Clinac 4's contribution to the war on cancer, they will have earned the gratitude of many others.



Twenty-two Clinac 4's are now on order. For further information, contact Varian Radiation Division, 611 Hansen Way, Palo Alto, California 94303; Springfield, New Jersey 07081; Varian A.G., Zug, Switzerland.

varian
radiation
division

What's so special about Halsey Film Dryers?...



The climate compensator control!



Model No. 601-D



Model No. 600-D

It solves the humidity problem!

The biggest bugaboo of film dryers is humidity in the darkroom . . . environmental moisture which turns the most efficient unit into a sluggish, slow-acting flop.

Now HALSEY introduces the *climate compensator* – a system of air control that lets you shut out outside humidity when it's too high . . . or bring in outside air when it's cool and dry.

The result . . . faster film drying – regardless of climate conditions!

No. 600-D. Fatigue-free loading from the top. Handles 12 films every 20 minutes. Complete with automatic timer — a guard against fire hazard due to failure to turn off the heater. Dimensions: 23″ wide, 33″ high, 17½″ deep.

No. 601-D. Economy version of above — loads from the front. Recommended for stacking on top of No. 600-D for stoop-free loading, when extra capacity is desired. Dimensions: 23″ wide, 33″ high, 17½″ deep. Automatic Timer (No. 602-DT) available.

No. 601-D-H. For restricted space — similar to No. 601-D, but almost 10″ narrower; accommodates 6 films. Dimensions: 13½″ wide, 33″ high, 17½″ deep.

Through your dealer

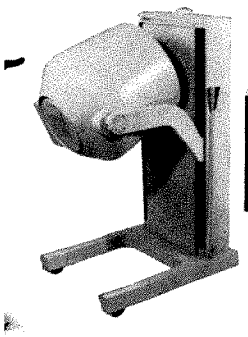
HALSEY

HALSEY X-RAY PRODUCTS, INC.
1425-37th STREET, BROOKLYN, N.Y. 11218

CHICAGO: 7321 Monticello Avenue, Skokie, Illinois 60076
LOS ANGELES: 1816 W. 8th St., Los Angeles, Calif. 90057

Unlike other scintillation cameras, Baird-Atomic's Autofluoroscop features computer-type memory. And that's saying a lot.

It says our non-volatile magnetic core memory can store raw digital data for each picture element. And *restor* image plane uniformity. It lets you flag any areas of the picture for numerical integration in dynamic studies. permits fast storage on magnetic tape to provide more data points in dynamic studies. It lets you play back patie data in its original form at any time. Instantly. And because of magnetic co memory, the picture has the same integrity as the raw data. The fact is, magnet core storage makes the Autofluoroscope a fundamentally more practical and ob jective tool. What's more, it's faster and easier to use in all procedures than oth cameras. So if you're going to buy or lease an imaging device, you should talk Baird-Atomic before you make your final decision. You owe it to yourself to ful understand why the tiny difference will make such a big difference to your pr gram. Naturally, if you're not already thinking about the Autofluoroscope, we ma not change your mind. But we'll give you a tough decision make. Call for an appointment. 33 University Road, Cambridg Massachusetts 02138, Telephone: 617 864-7420. Baird-Atomi Europe, The Hague, The Netherlands. Baird-Atomic Limited, Hornchurch, England.

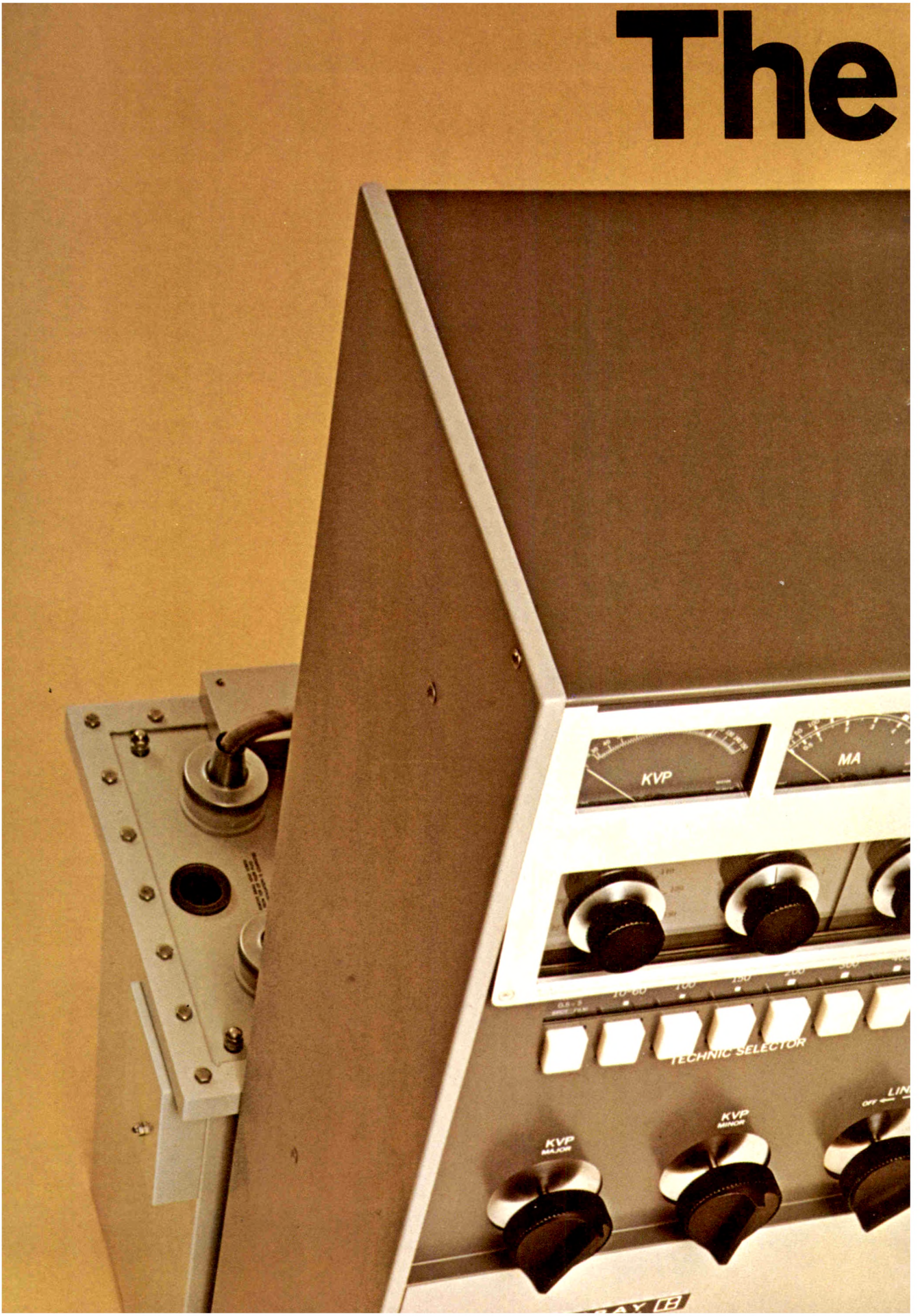


BA BAIRD-ATOMIC

The tiny difference.



The



Lightweight.



Some people seem to think x-ray generator should be sold by the pound. That if one backu circuit is good, then three make it even better

Nonsense.

The more spaghetti you put inside one of these things, the more you've got that can go wrong with it. Excess circuitry leads to just one result: excess downtime

So this Profexray generator—and all ou other equipment—is engineered t cut out electronic redundancy. O course, all the necessary backu systems are there. But it's a littl lighter in weight than most. And on heck-of-a-lot more reliable

Notice too, please, that our transforme isn't chubby like all the others. Whic makes it fit handily under a cabine somewhere, instead of in the basemen

Before you buy or specify any nev equipment, let us show you the muscle i one of our lightweights

Without an ounce of fat.

Litton Medical Products
A Litton Industries Group, Profexray Divisio
515 East Touhy Avenue – Des Plaines, Illinois 6001

New Radiology Titles
From Warren H. Green, Inc.

OCCULT TRAUMATIC LESIONS OF THE CERVICAL VERTEBRAE—Martin Abel, M.D., *Formerly, Dept. Radiol., Jefferson Med. Coll.* 1969, about 160 pp., 150 ill. **about $9.25**

PRACTICAL APPLICATIONS OF PHYSICS TO RADIOLOGY AND NUCLEAR MEDICINE—Carl R. Bogardus, Jr., M.D., *Director, Div. Rad. Therapy, Dept. Radiol., Univ. Oklahoma Med. Center* 1969, 240 pp., 240 ill. **$12.75**

CANCER OF THE URINARY BLADDER: With Emphasis on Treatment by Irradiation—William L. Caldwell, M.D., *Director, Radiotherapy and Radiation Res., Vanderbilt Univ. Hosp.* 1969, 156 pp., 30 ill. **about $7.50**

THE CHEST FILM IN PULMONARY HYPERTENSION—C. H. Joseph Chang, M.D., *Dept. Radiol., Med. Center, Sch. of Med., West Virginia Univ.* 1969, about 272 pp., 60 ill. **about $12.75**

ATLAS OF ROENTGEN ANATOMY OF THE NEWBORN AND INFANT SKULL: With Illustrations of Some Pathologic Changes and Congenital Variations—Charles N. Chasler, M.D., *Clin. Prof. Radiol., Univ. Pittsburgh Med. Center, and Consulting Radiologist, Western Psychiat. Inst. and Clin., Magee-Womens Hosp.* 1969, about 224 pp., 225 ill. **about $12.50**

SELECTIVE ARTERIOGRAPHY OF SPINAL CORD VESSELS: With Particular Regard to Arteriovenous Aneurysms—John L. Doppman, M.D., *Dep. Chief, Dept. Diag. Radiol., NIH, and Asst. Prof. Radiol., Johns Hopkins Univ. Sch. Med.;* Giovanni Di Chiro, *Head, Sect. Neuroradiol., Med. Neurol. Branch, NIH, and Prof. Radiol., Georgetown Univ. Sch. Med.; and* Ayub K. Ommaya, M.B., *Assoc. Neurosurgeon, Surg. Neurol. Branch, NIH, and Hunterian Prof., Roy, Coll. Surg. Engl.* 1969, 224 pp., 147 ill. (6 color), **$12.50**

CLINICAL CARDIAC ROENTGEN DIAGNOSIS—Alphons Jacob, M.D., *Head, Dept. Radiol., Coltzea Teaching Hosp. and Clin., Asst. Chairman, Postgrad. Med. Sch., Bucarest, Romania* 1969, about 384 pp., 289 ill., 38 tab. **about $15.75**

THE NEGLECTED CAUSE OF STROKE: Occlusion of the Smaller Intracranial Arteries and Their Diagnosis by Cerebral Angiography—B. Albert Ring, M.D., *Depts. Anat. and Radiol., Univ. Vermont Coll. Med.* 1969, 224 pp., 145 ill. **$10.50**

THE APPLICATION OF RADIOIODINATED ROSE BENGAL AND COLLOIDAL RADIOGOLD IN THE DETECTION OF HEPATOBILIARY DISEASE—Leonard Rosenthall, M.D., *Director, Div. Nuclear Med., Dept. Radiol., Montreal Gen. Hosp.* 1969, 196 pp., 199 ill. **$9.25**

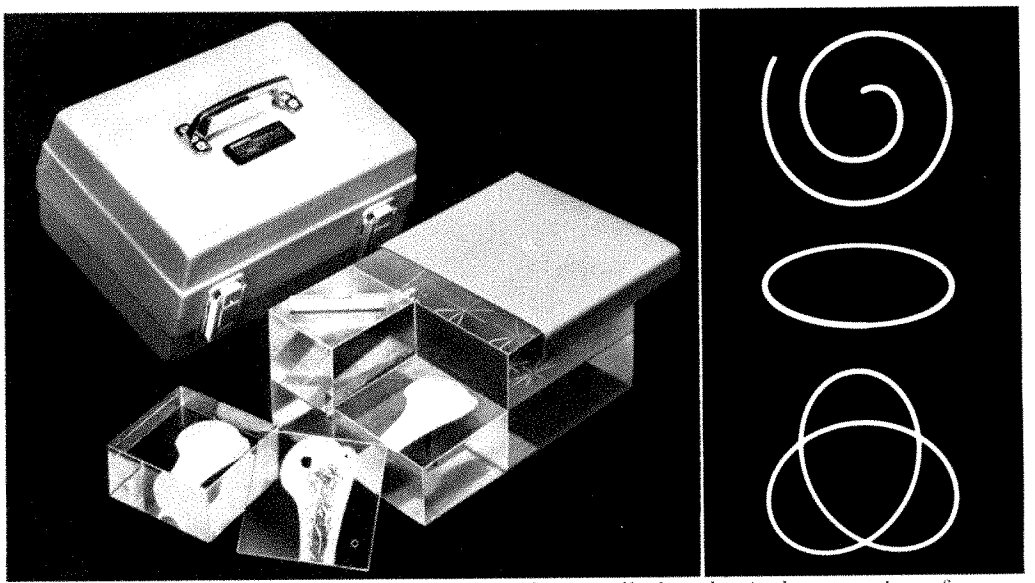
CORONARY DISEASE MANAGEMENT: Coronary Arteriography, Nitrates, and the Triple Pedicle Operation—William H. Sewell, M.D., *Guthrie Clin.* 1969, about 200 pp., 80 ill. **about $10.00**



WARREN H. GREEN, INC.
Publisher

10 SO. BRENTWOOD BLVD.
ST. LOUIS, MISSOURI 63105

Announcing a new first. The 3M Tomographic Phantom



Now a single tomographic phantom that evaluates all the physical properties of your tomographic device.

With the 3M Tomographic Phantom you can examine all of the critical properties of your tomographic device . . . such as:

- GEOMETRIC FORM OF BLUR
- MECHANICAL STABILITY
- COMPLETENESS OF EXPOSURE
- VARIATION IN INTENSITY
- PENDULAR ANGLE
- ORIENTATION OF THE MOVEMENT
- SECTION THICKNESS
- CHANGE OF FOCAL PLANE
- DISTORTION
- QUALITY OF BLUR
- RESOLUTION
- COMPLETENESS OF MARGINAL OCCURRENCES
- ACCURACY OF TOMOGRAPHIC IMAGE

Phantom is protected by a specially designed carrying case. Complete instructions for use. Available only through manufacturers and distributors of tomographic devices.

Photographic Products 3M COMPANY

3M CENTER • ST. PAUL, MINNESOTA 55101



This "cow" stands out from the herd!

This is Pertgen-99m, the cow that doesn't leak. Nothing comes out until you're ready to milk it.

Yields are consistent and high—an unbeatable combination!

Safety—underneath the Pertgen-99m Generator is the Rayshield™, Abbott's exclusive Radioisotope Shielded Dispensing Unit, that keeps radiation to operating personnel at a minimum.

Convenience—the protection afforded by the unique Rayshield means that Pertgen-99m can be used on the lab bench—there's no need to hide this system behind the bricks!

Economy—because Pertgen-99m is precalibrated, you get more useable activity at no increase in cost!

PERTGEN™-99m

TECHNETIUM Tc 99 GENERATOR KIT

Also available:

PERTSCAN™-99m

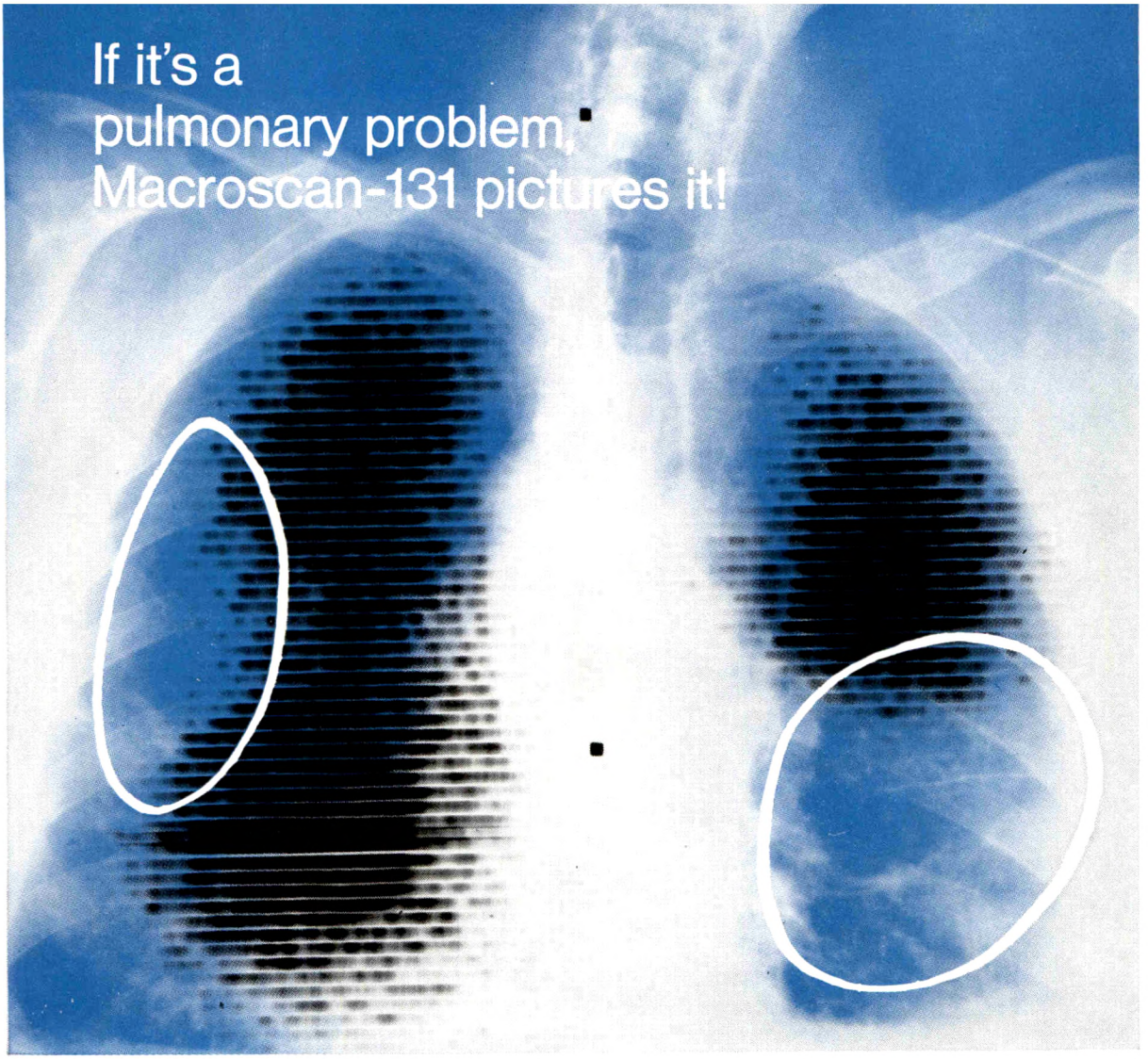
SODIUM PERTECHNETATE Tc 99m

Abbott Laboratories North Chicago, Illinois 60064

World's Leading Supplier of Radio-Pharmaceuticals

LABOR-SERVICE GMBH, Abteilung RADIO-PHARMAZEUTIKA,
6236 Eschborn/Ts, Frankfurter Str. 20, Postfach 1245

If it's a pulmonary problem, Macroscan-131 pictures it!



A 70-year old man was admitted unconscious to the intensive care unit. Studies failed to reveal evidence of a myocardial infarction and the X-ray was not revealing. A pulmonary infarct was suspected and this diagnosis was established by a lung scan.

His posterior view scan above, showing diminished uptake in the left lingula and right lower lobe, was made with Macroscan-131. This product has many diagnostic uses:

Pulmonary embolism, suspected: To confirm (or rule out) its occurrence.

Chronic pulmonary tuberculosis: To estimate unilateral and regional function and perfusion of the lungs.

Emphysema: To evaluate the decreased regional blood flow that occurs with obstruction of vessels.

Pneumonitis: To evaluate the decreased regional blood flow that occurs without obstruction of vessels.

Lung Tumors: To evaluate the regional ischemia resulting from compression or obstruction of pulmonary arteries.

Surgery and/or other therapy for lung disorders: To evaluate the effectiveness of therapeutic measures.

Macroscan-131 is sterile and non-pyrogenic. It is ready to use and should not be heated prior to use.

INDICATIONS: For scintillation scanning of the lungs to evaluate total, unilateral, and regional arterial perfusion of the lungs.

CONTRAINDICATIONS: Radio-pharmaceutical agents should not be administered to pregnant women or to persons less than 18 years old unless the indications are very exceptional.

PRECAUTIONS, SIDE EFFECTS: Care should be taken to administer the minimum dose consistent with safety and validity of data. The possibility of an immunological response to albumin should be kept in mind when serial scans are performed. There is a theoretical hazard in acute cor pulmonale, because of the temporary small additional mechanical impediment to pulmonary blood flow. A possible case of urticaria has been related to a similar preparation. The thyroid gland should be protected by prophylactic administration of concentrated iodide solution. 903116

Macroscan™-131

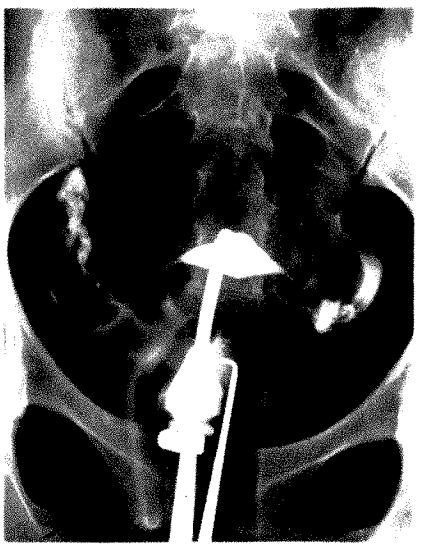
AGGREGATED RADIO-IODINATED (I^{131}) ALBUMIN (HUMAN)

ABBOTT LABORATORIES
North Chicago, Illinois 60064

World's Leading Supplier of Radio-Pharmaceuticals
LABOR-SERVICE GMBH, Abteilung RADIO-PHARMAZEUTIKA,
6236 Eschborn/Ts, Frankfurter Str. 20, Postfach 1245



MEDOPAQUE



Sterile, aqueous, viscous Medopaque offers optimal radiopacity and complete absorption in 45 minutes from mucous and serous surfaces. Miscible with body secretions, spreads without droplet formation. Safe in the event of intravasation. In vials of 10 cc.

For

Hysterosalpingography
Cholangiography (operative and t-tube)
Biliary Ducts
Fistulous Tracts

Medopaque contains 35% sodium ortho-iodohippurate, 10% sodium iodide, with added stabilizer, preservatives and a blend of polyethylene glycols.

Professional sample supply available on request.

BELL-CRAIG, INC.

41-14 27th Street L.I.C., N.Y. 11101

we wouldn't leave "well enough" alone!

improved Albumotope®—LS

Aggregated Radio-Iodinated (I^{131}) Albumin (Human) for Lung Scanning

introduced by Squibb...
improved by Squibb

■ Reduced Protein Content

Squibb has reduced the amount of protein by 50% while maintaining good lung scans.

■ Reduced Supernatant Activity

Squibb has sharply reduced the amount of radioactivity in the supernatant, decreasing the possibility of liver interference with the lung scan.

■ Reduced Unbound Iodine

Squibb has substantially reduced the amount of unbound iodine 131, effectively reducing the problem of blood background radioactivity.

Albumotope—LS—a good example of Squibb leadership in radiopharmaceutical research and development. Some people won't leave "well enough" alone.

Contraindications: Radiopharmaceuticals should not be administered to pregnant women or to persons under the age of 18 years unless the indications are very exceptional. Because iodide is excreted in human milk, aggregated radioalbumin should not be administered to nursing mothers.

Side Effects and Precautions: There have been no reported cardiovascular or other untoward effects attributable to Albumotope—LS. Extensive clinical use of Albumotope—LS has not borne out the hypothetical possibility that particles of large size might induce deleterious cardiovascular or cerebrovascular effects. The product appears to possess no antigenic properties. One patient with a known history of angioneurotic edema, who had been given Lugol's solution in conjunction with aggregated radioalbumin similar to Albumotope—LS, developed urticaria.

For full prescribing information, see package insert.

Available: As a sterile, nonpyrogenic, aqueous suspension. Each cc. contains approximately 0.5 mg. aggregated human serum albumin labeled with iodine 131. Not less than 90% of the aggregates are between 10 and 90 microns and none are more than 150 microns in size. The preparation also contains 0.9% (w/v) benzyl alcohol as a preservative. The potency ranges from 250 to 450 microcuries per cc. on date of assay.

Medotopes®

SQUIBB Division of Nuclear Medicine
East Brunswick, New Jersey 08816

The no-mix.

We took the construction work out of barium sulfate.

We premixed it into a smooth, creamy, instantly ready esophageal contrast medium.

Before, coating was often a hit-or-miss operation ('home-brewed' barium can be too thin, too thick or just plain settled out).

Not anymore.

Now, in seconds, you can photograph your patient's esophageal tract...easily take 3, 4, even 5, plates after an initial dose. In many patients the coating of Esophotrast lasts up to 15 minutes (ample time for fluoroscopy and radiography of the esophagus and evaluation of heart size).

Now you don't have to cajole your patients into drinking cupful after cupful of barium...the 1 oz. of Esophotrast, usually all that's needed, is nongritty and fruit-flavored–a really pleasant medium to take.

And it's just a squeeze of a tube away.

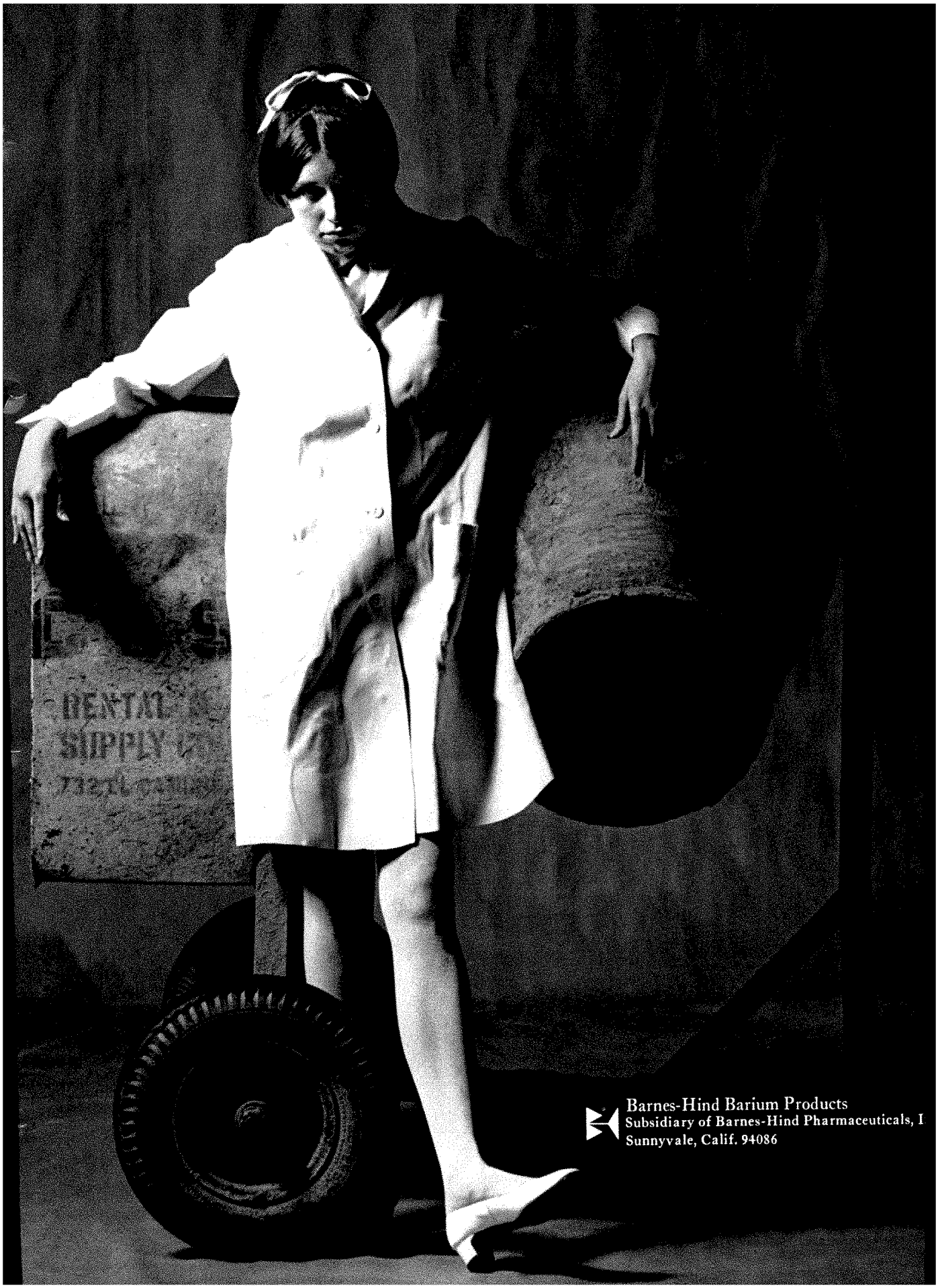
So why mix your own?

Esophotrast®

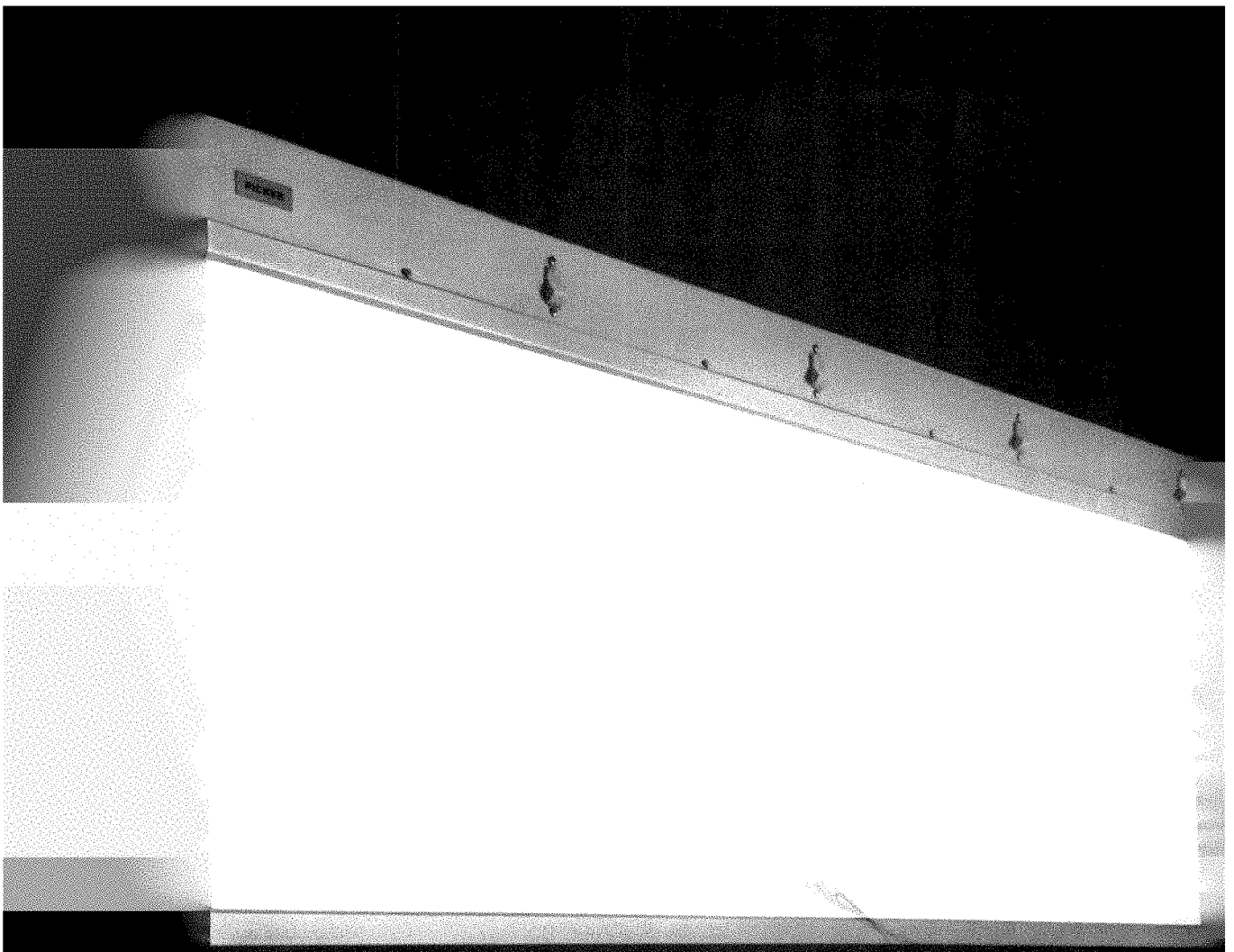
(barium sulfate)

Instantly ready esophageal cream

Recommended dose: 1 tablespoonful "chewed" thoroughly before swallowing. Repeat with a second tablespoonful to ensure prolonged adherence and coating of the esophageal mucosa.



Barnes-Hind Barium Products
Subsidiary of Barnes-Hind Pharmaceuticals, I
Sunnyvale, Calif. 94086



Hang up extra brightness with a handsome "built-in" look.

er's new easy-mount THINBRITE x-ray illuminator needs no costly "installation"—you simply
it up wherever and whenever you need film-viewing capability. Comes in units with 1, 2, 3, or 4
x 17" viewing surfaces in an uninterrupted sweep of light. Once up, it lies so flat to the wall (the
x sides project only 3-11/16") that a THINBRITE mount is hard to tell from an expensively built-in
inator.

INBRITE gives you all this with the bonus of extra brightness, too: the more efficiently distrib-
output of a quartet of fluorescent tubes (instead of the usual two or three) increases overall
tness up to 50% above conventional levels.

w to learn more about how simple it is to handsomely expand your viewing facilities, call your
Picker representative or write the Picker Corporation.

1275 Mamaroneck Avenue, White Plains, New York 10605. **PICKER**

SIEME

From our total commitment

X-ray diagnosis, radiotherapy, nuclear medicine, medical data proces
We are engaged with the entire spectrum of medical technology.
Our research and development people keep close liaison with medica
research and practice, consequently, we are able to offer the physicia
equipment tailored for his specific tasks.



SIEMENS MEDICAL OF AMERICA INC.
685 LIBERTY AVENUE, UNION, N.J. 07083

SIEMENS

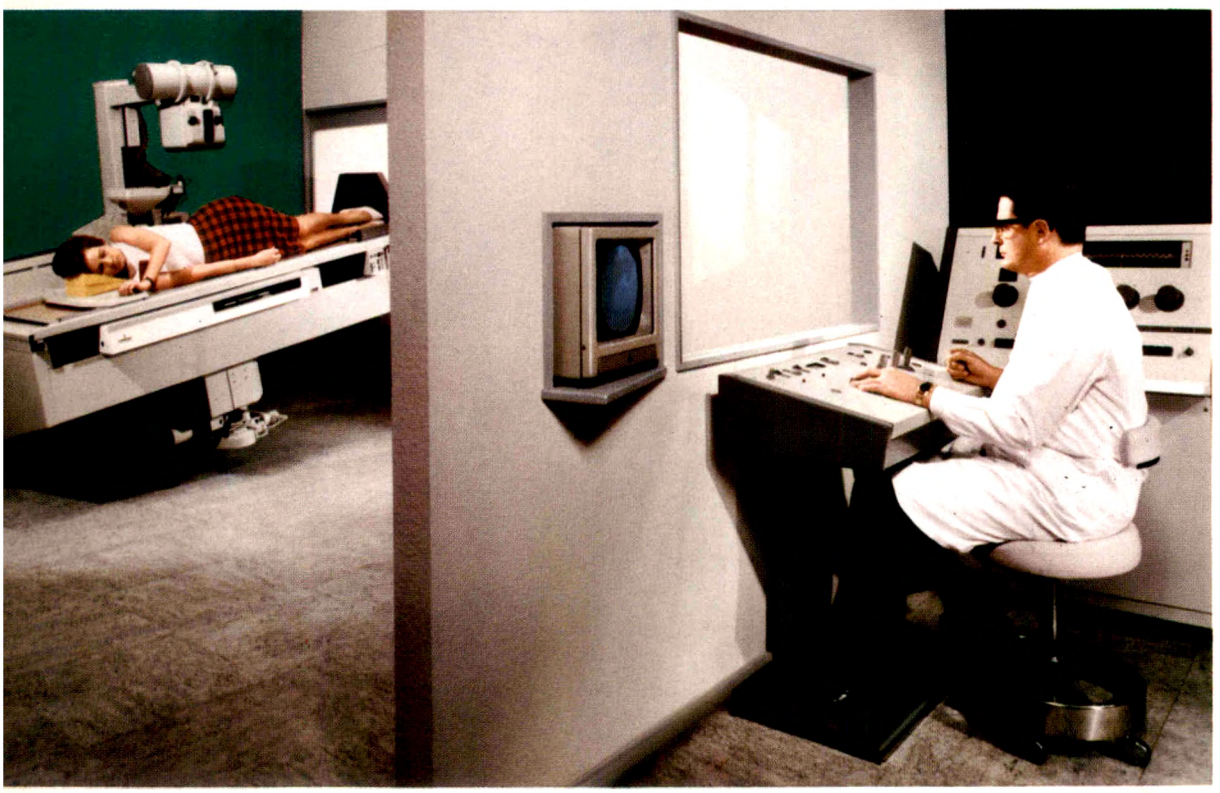
GRAPH System Approach

; remote control console to the smallest table
ory, the SIREGRAPH is the „System Approach"
adiologists' most pressing problems – how to
he highest possible consistent quality of
tion and how to make the most efficient use
me.

ıding features include:
) continuously variable speed motor driven
ıble
ting cradle (optional)
way power top

- Fully automatic undertable spot film device for use with five various cassette sizes
- Built-in 10/6 SIRECON Image Intensifier with television which tracks the X-ray beam through all angulations of X-ray tube or table
- Routine and special techniques including planigraphy and zonography
- Choice of recording methods from image system 70 mm – 35 mm or 16 mm cine

SIEMENS MEDICAL OF AMERICA INC.
685 LIBERTY AVENUE, UNION, N. J. 07083



SQUIBB

a research concept in contrast visualization

for clear definition of disease:

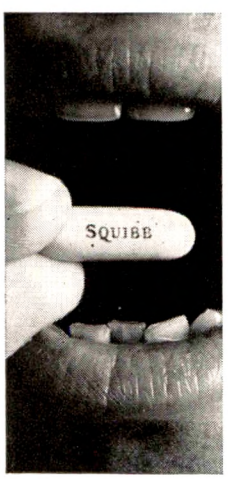
this oral medium is the message...

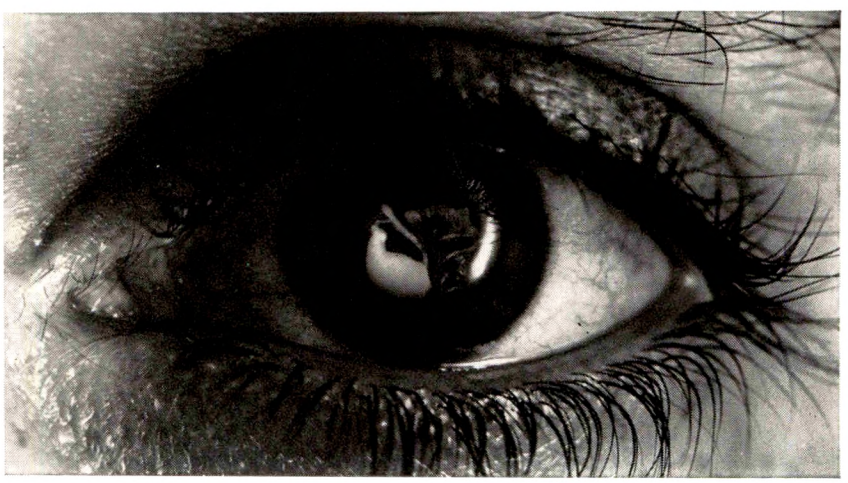
Oragrafin® Calcium (Squibb Calcium Ipodate) visualizes the gallbladder and ducts quickly and clearly with few undesirable reactions. For rapid or routine studies of the gallbladder and biliary ducts, Oragrafin permits efficient absorption for maximum concentration and excellent contrast—with bowel residue in only a small percentage of patients and few patient problems.

Oragrafin (Squibb Ipodate) in radiography — an advanced medium of biomedical communication. According to McLuhan's[1] provocative new theories of communications, all media are considered "extensions of man"—the means by which he extends his understanding and control of the universe and himself. In biomedical communications, where man monitors the diverse processes of molecular and cellular change, modern contrast radiography is an advanced medium.

Today, in cholangiography and cholecystography, as the medium becomes increasingly oral, the diagnostic message is clear, rapid, and convenient with Oragrafin (Squibb Ipodate).

For summary of contraindications, precautions, and side effects, see end of this advertisement.





the medium:

Oragrafin®

Squibb Ipodate

the message:

maximum concentration... excellent toleration

high absorption index—"No one will dispute the statement that the diagnostic reliability of oral cholecystography depends upon the degree of absorption of the contrast medium employed."[2] Radioisotope studies with ipodate sodium show a markedly improved absorption index (approximately 70 per cent) with no increase in the toxic properties.[2]

excellent opacification—"In addition to its ease of administration and safety, its principal advantages are a high yield of diagnostic films...."[3]

less bowel residue—"Incomplete and variable absorption of a cholecystographic agent is not desirable, for the opacification of the gallbladder is then less dependent on the status of the gallbladder and more a reflection of the percentage absorption."[4]

"Opaque material in the bowel was found in 46 per cent of [105 patients in] the ... [iopanoic acid] group as compared with 9 per cent of those [99] of the [Oragrafin Sodium Capsules] ... group."[4] In another study, 49 of 100 patients receiving iopanoic acid had residue in the gastrointestinal tract, while only 15 of 100 patients receiving Oragrafin Sodium Capsules had such residue.[5]

no evidence of nephrotoxicity, infrequent side effects—In contrast to findings with other cholecystographic agents, Lewitan and Garcia[6] reported in their 246-patient study: "With ipodate calcium ... there was no clinical evidence of immediate or delayed nephrotoxicity in any of the patients given it...."[6] To study possible renal toxicity, "Creatinine clearance tests were also done before and after administration of multiple doses in excess of 6 gm. in 8 cases, and showed no significant alterations."[6] However, "Multiple doses beyond 6 gm. are not recommended."[6]

In their study of 120 patients, Glenn and O'Brien reported "...no reactions in this series of patients attributable to the administration of [Oragrafin]...."[3]

And, McCrory reported that Oragrafin Sodium and Calcium was "...used routinely in cholecystographic studies in approximately 2000 patients with excellent diagnostic films and only rare and mild reactions."[7]

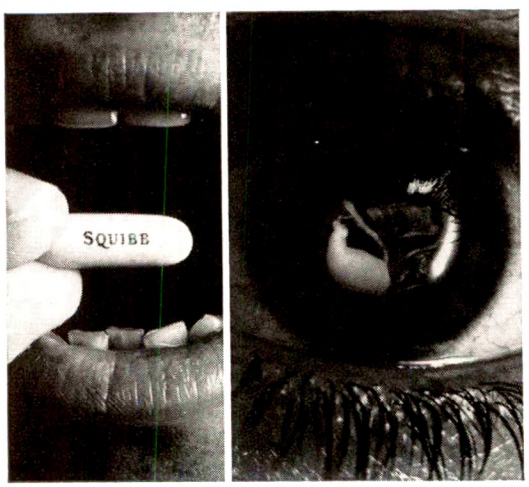
fewer side effects than iopanoic acid—According to White and Fischer,[4] 36 (36.4%) instances of side effects occurred in 99 cases with Oragrafin Sodium, 3 Gm. compared with 87 (82.9%) in 105 cases with iopanoic acid, 3 Gm. Kinds of side effects noted were nausea, vomiting, diarrhea, cramps and dysuria—all less frequent with Oragrafin Sodium (Squibb Sodium Ipodate).

Juhl,[5] in his study of 200 patients (100 on iopanoic acid and 100 on sodium ipodate), found that the incidence of nausea and vomiting was equal in the two groups.[5]

Oragrafin (Squibb Ipodate) dosage schedules
Oragrafin (calcium or sodium ipodate) permits overnight cholecystography and cholangiography.

	Gallbladder Films		Films of the Gallbladder and Biliary Ducts
11 P.M.	6 Capsules OR (or 12 Capsules)	1 packet of Granules (or 2 packets)	6 Capsules (or 1 packet of Granules, if preferred) and
next morning 8 A.M.			1 packet of Granules
9 A.M.	Visualization of gallbladder	Visualization of gallbladder	Visualization of ducts and gallbladder
10 A.M.			
11 A.M.			

For summary of contraindications, precautions, and side effects, see next page.



speed and convenience of Oragrafin® Calcium Granules

Squibb Calcium Ipodate

new clinical study[8] demonstrates improved diagnoses with calcium ipodate—"A group of 114 patients with poorly filled gallbladders after routine administration of iopanoic acid were given 6 gm. of [calcium] ipodate granules immediately following their routine cholecystography. In 66 per cent of these patients opacification of the gallbladders was obtained within 3 hours, allowing a definite diagnosis. Of the remaining 33 per cent, one-half were ultimately proven diseased." "It is apparent that many poorly visualized gallbladders can be rendered visible by the ingestion of ipodate granules.... A whole day may be saved and other diagnostic studies may be performed."[8]

patient convenience—Routine cholecystography night-before procedure is easy for patients to follow; palatable granules further enhance patient acceptability. Rapid clearance of medium permits same-day administration and gallbladder and ductal films, and if necessary, same-day re-examination; reduces need for I.V. studies.

rapid absorption permits same-day re-examination—To determine the cause of nonopacification after routine cholecystography using 6 capsules, physicians may require re-examination by repeating the procedure at a later date (sometimes doubling dose to 12 capsules), or by administering more agent the evening of the first unsuccessful examination (again sometimes doubling dose to 12 capsules), and repeating the study the next day. "The advantage of the calcium ipodate method is that the examination can be completed in five additional hours with a limited dose of contrast agent."[9]

"a valuable medium for peroral cholegraphy"[6]—Rapidly absorbed from the gastrointestinal tract, calcium ipodate has been reported by some investigators to be diagnostically superior to other oral cholangiographic contrast agents.[10,11] With careful timing of the examination and the use of tomograms or laminograms, the frequency of good results can approximate that obtained with intravenously administered agents.[10] According to Lewitan and Garcia,[6] the medium's relative safety makes it a valuable medium for peroral cholegraphy. Timesaving and economical Oragrafin Calcium Granules may be particularly useful in certain patients for whom I.V. radiography presents potential hazards, such as elderly patients and those with cardiovascular disease.

Unique among oral media, Oragrafin Calcium Granules permits same-day films of the gallbladder and the ductal system.

dosage schedule for films of gallbladder and ductal system

8 A.M.	2 packets of granules
9 A.M.	visualization of ducts
10 to 11 A.M.	visualization of gallbladder

Contraindications: Contraindicated for persons sensitive to oral iodine compounds or for patients with *combined* renal and hepatic disease or *severe* kidney impairment. Gastrointestinal disorders, which may interfere with absorption, or liver dysfunction, which may result in inadequate biliary secretion of medium, are likely to result in unsatisfactory visualization.

Precautions and Side Effects: Mild and transient nausea, vomiting, or diarrhea sometimes occur; but the incidence can be reduced by using the calcium granules and restricting the dosage to 3 Gm. Transient headache, dysuria, or abdominal pains may occur.

Hypersensitivity reactions may include urticaria, serum sickness-like reactions, and rarely anaphylactoid shock. They are more likely to occur in the individual with a history of allergy, asthma, hay fever, or urticaria and in the individual who is known to be hypersensitive to iodine compounds. Antihistamines and corticosteroids are used to control hypersensitivity reactions; but the occasional serious anaphylactoid reactions require the immediate use of epinephrine or phenylephrine, oxygen, and intravenous corticosteroids.

For full information see Package Insert.

Supply: The calcium salt (Oragrafin Calcium Granules) is available in single-dose foil packets providing 3 Gm. of calcium ipodate as Granules dispersed in flavored sucrose. The sodium salt is available in capsule form (Oragrafin Sodium Capsules) providing 0.5 Gm. sodium ipodate per capsule.

References: 1. McLuhan, M.: Understanding Media: The Extensions of Man, New York, McGraw-Hill Book Company, 1966. **2.** Sanen, F. J.: Amer. J. Roentgen. *88*:797 (Oct.) 1962. **3.** Glenn, J. C., Jr., and O'Brien, P. S.: Southern Med. J. *56*:167 (Feb.) 1963. **4.** White, W. W., and Fischer, H. W.: Amer. J. Roentgen. *87*:745 (April) 1962. **5.** Juhl, J. H., *et al.*: Radiology *80*:87 (Jan.) 1963. **6.** Lewitan, A., and Garcia, J. F.: Amer. J. Dig. Dis. *10*:219 (March) 1965. **7.** McCrory, E.: J. Tenn. Med. Ass. *58*:258 (Aug.) 1965. **8.** Root, H.: Amer. J. Roentgen. *101*: 621 (Nov.) 1967. **9.** Crummy, A. B.: Wisconsin Med. J. *65*:84 (Feb.) 1966. **10.** Saltzman, G. F.: Acta Radiol. *54*: 417, 1960. **11.** Ludin, H., and Lauchenauer, C.: Schweiz. Med. Wochenschr. *90*:471, 1960.

for clear definition of disease: in oral cholangiography and cholecystography

Oragrafin®

Squibb Ipodate

SQUIBB

'The Priceless Ingredient' of every product is the honor and integrity of its maker.

A 2810

Laurel *and* Hardy. Inseparable. Made for each other.

The same goes for a nuclear-medicine department. Only *one* imaging system goes with it—is made for it—brings the department to its full potential.

Some things simply belong together.

Only the Pho/Gamma® III Scintillation Camera by Nuclear-Chicago. Only the Pho/Gamma III has the in-vivo visualization capabilities, the full range of data displays and data-manipulation accessories for today—and tomorrow.

Which is why more and more nuclear-medicine departments are going with and growing with the Pho/Gamma III. And helping to make it, now more than ever, *the world's most experienced scintillation camera.*

Call your Nuclear-Chicago sales engineer. Or write to us for full details on the Pho/Gamma III.



NUCLEAR-CHICAGO

A SUBSIDIARY OF G. D. SEARLE & CO.

2000 Nuclear Drive, Des Plaines, Illinois 60018, U.S.A.
Donker Curtiusstraat 7, Amsterdam W. The Netherlands
OM-103

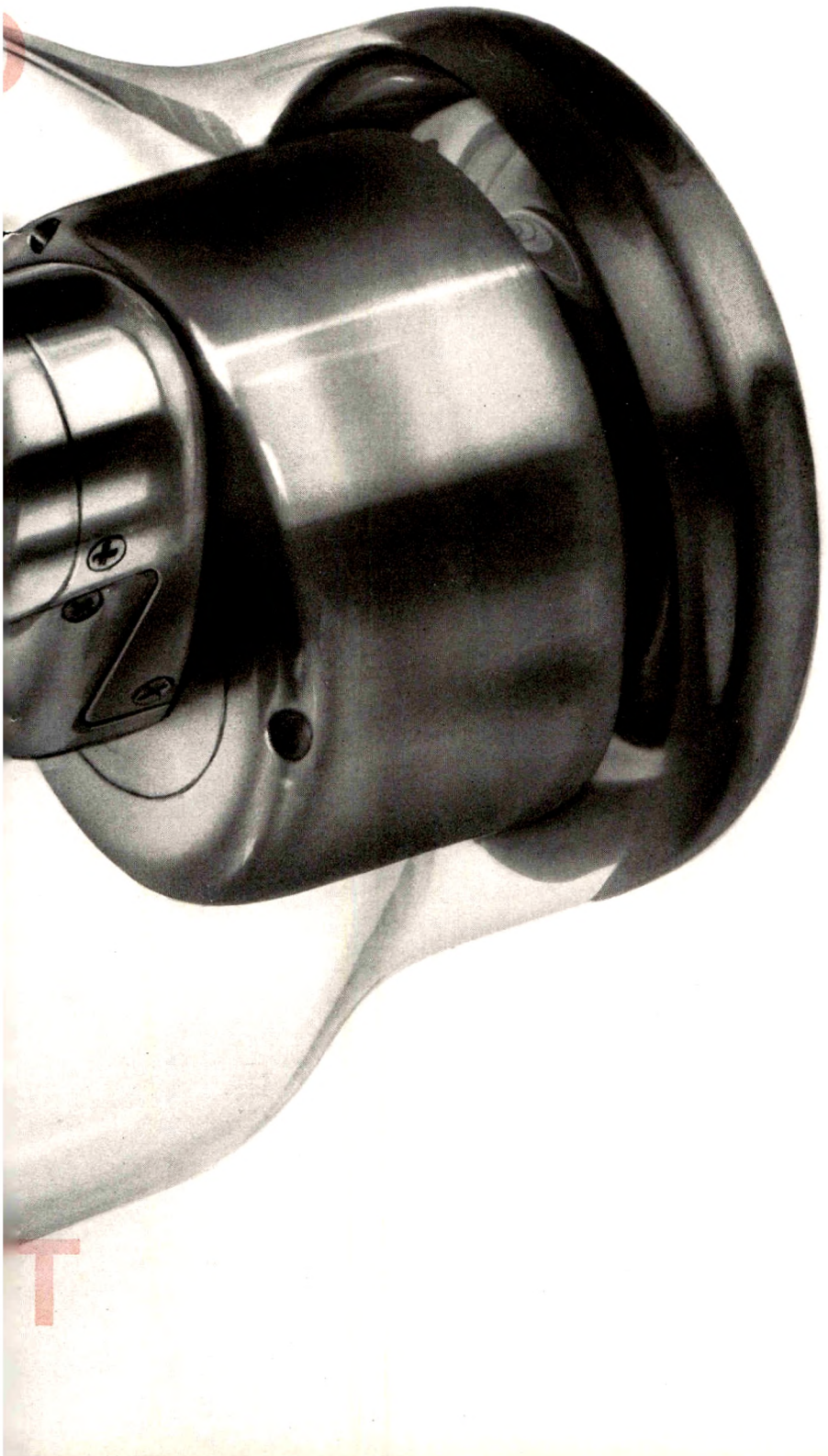


CULVER PICTURES

A NEW LINE OF HEAVY ROTATING ANODE X-RAY THAT LAST AND LAST



DUTY TUBES



the remarkable new DURATRONS by DUNLEE

Designed to fit most housing

Today's X-ray department. More traffic. More sophisticated. More exposures per hour. Someone had to develop an X-ray tube insert to meet the demands of today's radiology.

Dunlee did.

Superbly engineered, the Dunlee Duratron 175 and 140 rotating anode tubes have a high heat storage capacity, 175,000 H.U. on the 175 and 140,000 H.U. on the 140. Their high dissipation rate makes them applicable for all types of fluoroscopic, spot film and general radiographic service.

Specially constructed targets (rhenium-tungsten-molybdenum on the Duratron 175, enlarged solid tungsten on the 140) assure a tube life unsurpassed in the industry.

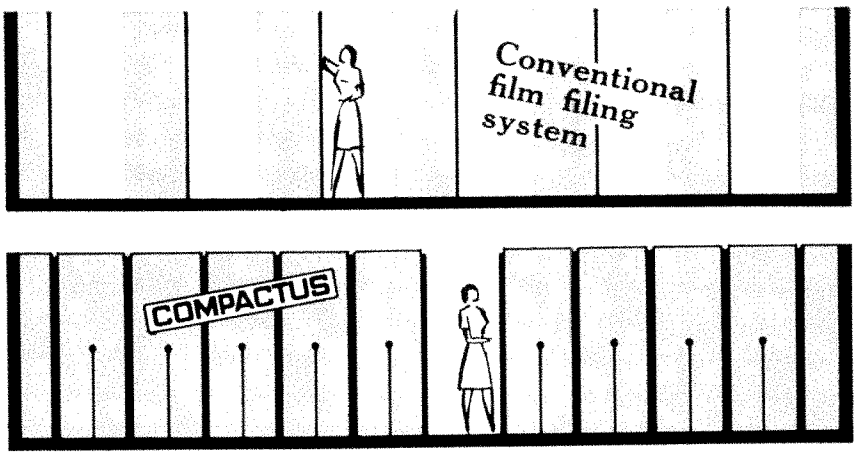
Specify the X-ray tube insert designed for today's radiology. Duratron by Dunlee. As a new tube unit with its own Duratron housing or as a replacement tube in most housings.

WARRANTY

Dunlee's Material and Workmanship Warranty is our expression of confidence and your assurance of the highest production and inspection standards.

Learn more about the benefits of the new Duratrons by Dunlee Ask your X-ray dealer or write.

DUNLEE CORPORATION
A PICKER CORPORATION SUBSIDIARY
1023 SOUTH CERNAN DRIVE
BELLWOOD, ILLINOIS 60104



COMPACTUS
MOBILE STORAGE SYSTEM

provides more X-Ray film storage for you!

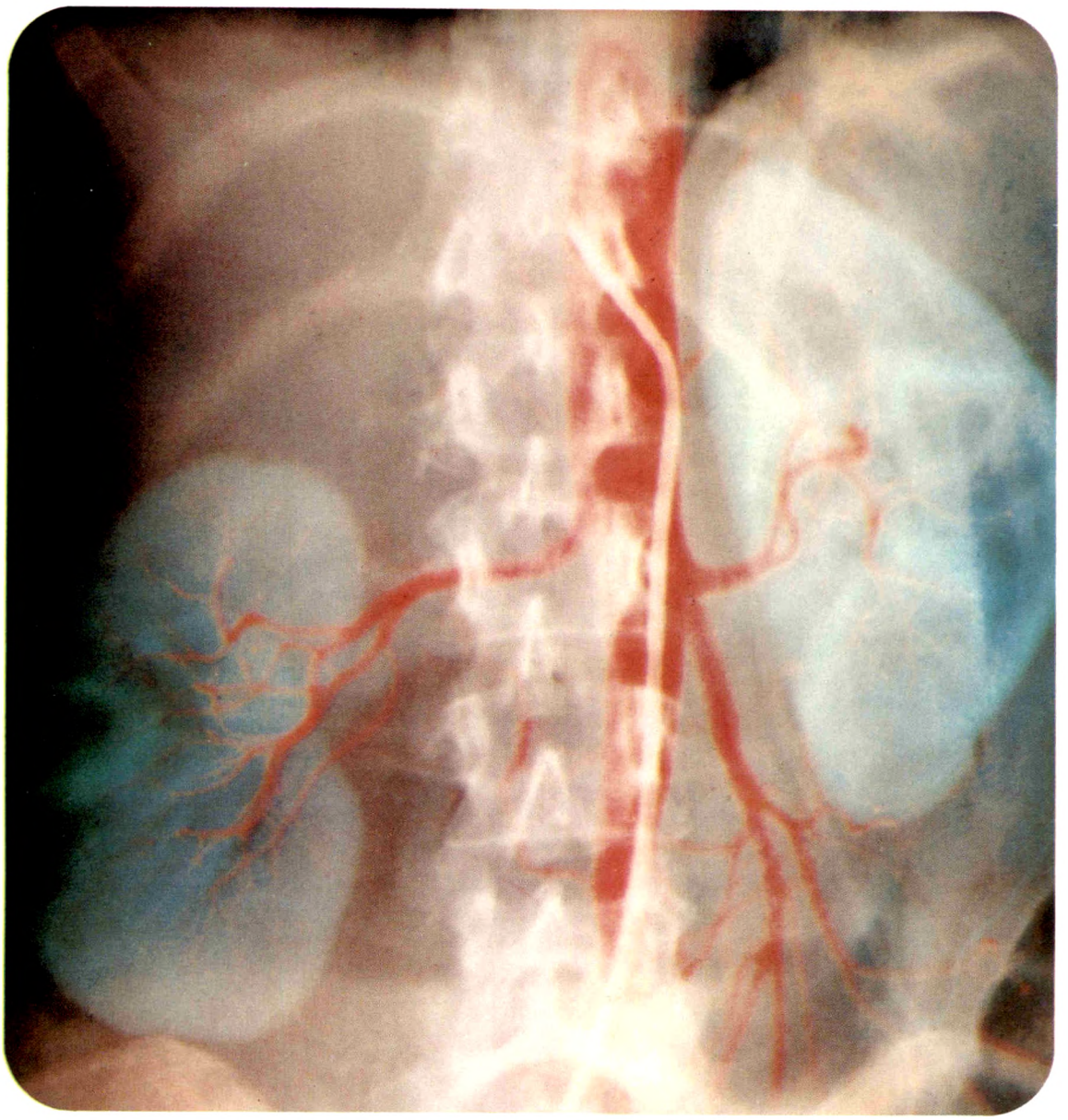
We will show you how
Compactus can increase
the capacity of
your storage space.
Please send us
a sketch of
your floor plan.

SCHICK
X-RAY

SCHICK X-RAY CO., INC.
415 Green Bay Road • Wilmette, Ill. 60091
Phone (312) 256-4700

Aortography

(percutaneous retrograde catheter technique) using Hypaque® sodium 50% as the contrast medium



The six color films illustrated, in which Hypaque was used as contrast medium, were supplied through the courtesy of Robert E. Wise, M.D. of the Lahey Clinic Foundation and New England Baptist Hospital, Boston, Mass. The technique, employing ordinary x-rays, is described in the Lahey Clinic Foundation Bulletin *14*:131, 1965.

and you'll get the same precise black-and-white definition using

Hypaque® 50%

sodium

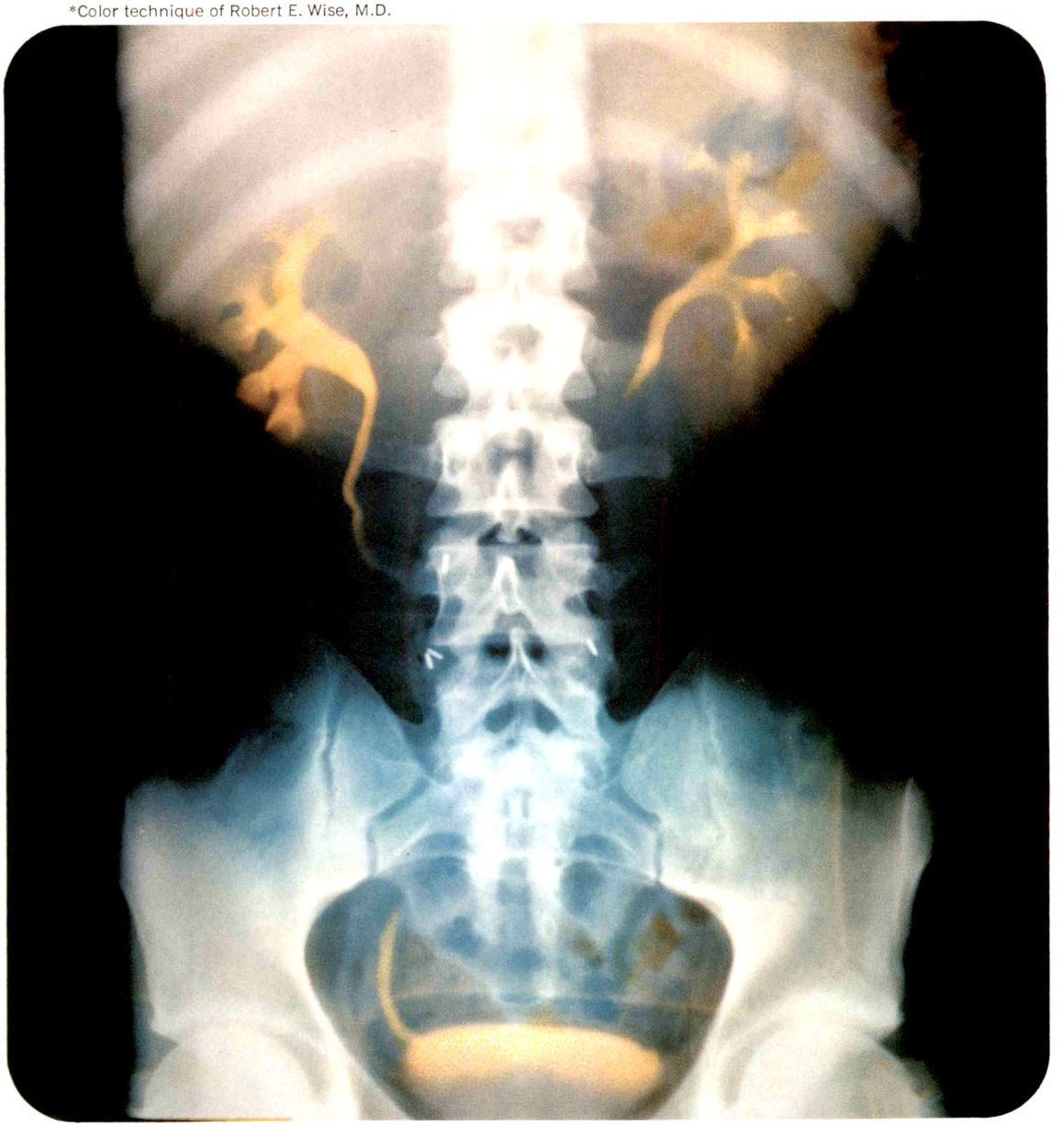
brand of **sodium diatrizoate**

Aortography with Hypaque sodium 50% may give valuable evidence in cases of renal agenesis, duplications or ectopia, or of polycystic kidney. Aortograms are also of importance in helping to demonstrate aneurysmal change or the degree of patency of the arteriosclerotic vessel, and in aiding the surgeon to determine proper surgical management if such is needed especially where a stenotic vessel is responsible for life-threatening renal hypertension. Aortograms with Hypaque 50% have provided clearly defined needed evidence of pathology prior to surgical intervention.

Excretory Urography

using Hypaque® sodium 50% as the contrast medium*

*Color technique of Robert E. Wise, M.D.



and you'll get the same precise black-and-white definition using

Hypaque® 50%
sodium
brand of **sodium diatrizoate**

Excretory urography with Hypaque sodium 50% provides the detection of urinary tract lesions, without interference with functional activity, without age limit and without anesthesia—important advantages when instrumentation is undesirable.

Cerebral Arteriography

using Hypaque® sodium 50% as the contrast medium*

*Color technique of Robert E. Wise, M.D.



and you'll get the same precise black-and-white definition using

Hypaque® 50%
sodium
brand of **sodium diatrizoate**

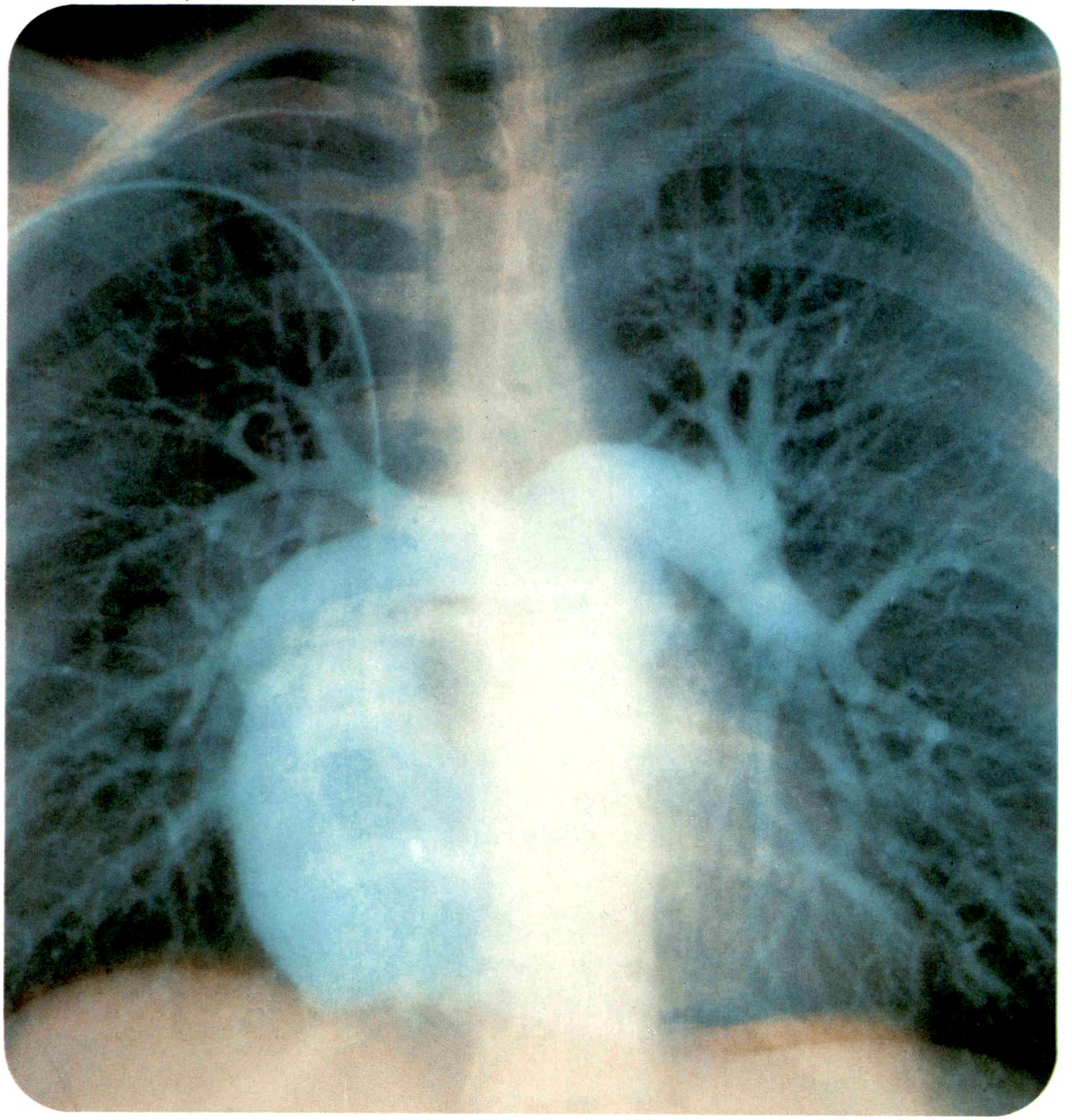
Cerebral arteriography with Hypaque sodium 50% has proved most useful in localizing and identifying intracranial lesions. Because it demonstrates both pathologic anatomy and physiology in such disorders as aneurysms, hematomas, angiomatous formations, meningiomas, glioblastoma multiforme, and other neoplasms, this procedure may provide diagnostic information frequently unobtainable by other means.

Please read the summary of prescribing information on the last pages of this unit

Angiocardiography

using Hypaque®-M, 75% as the contrast medium*

*Color technique of Robert E. Wise, M.D.



and you'll get the same precise black-and-white definition using

Hypaque®-M, 75%

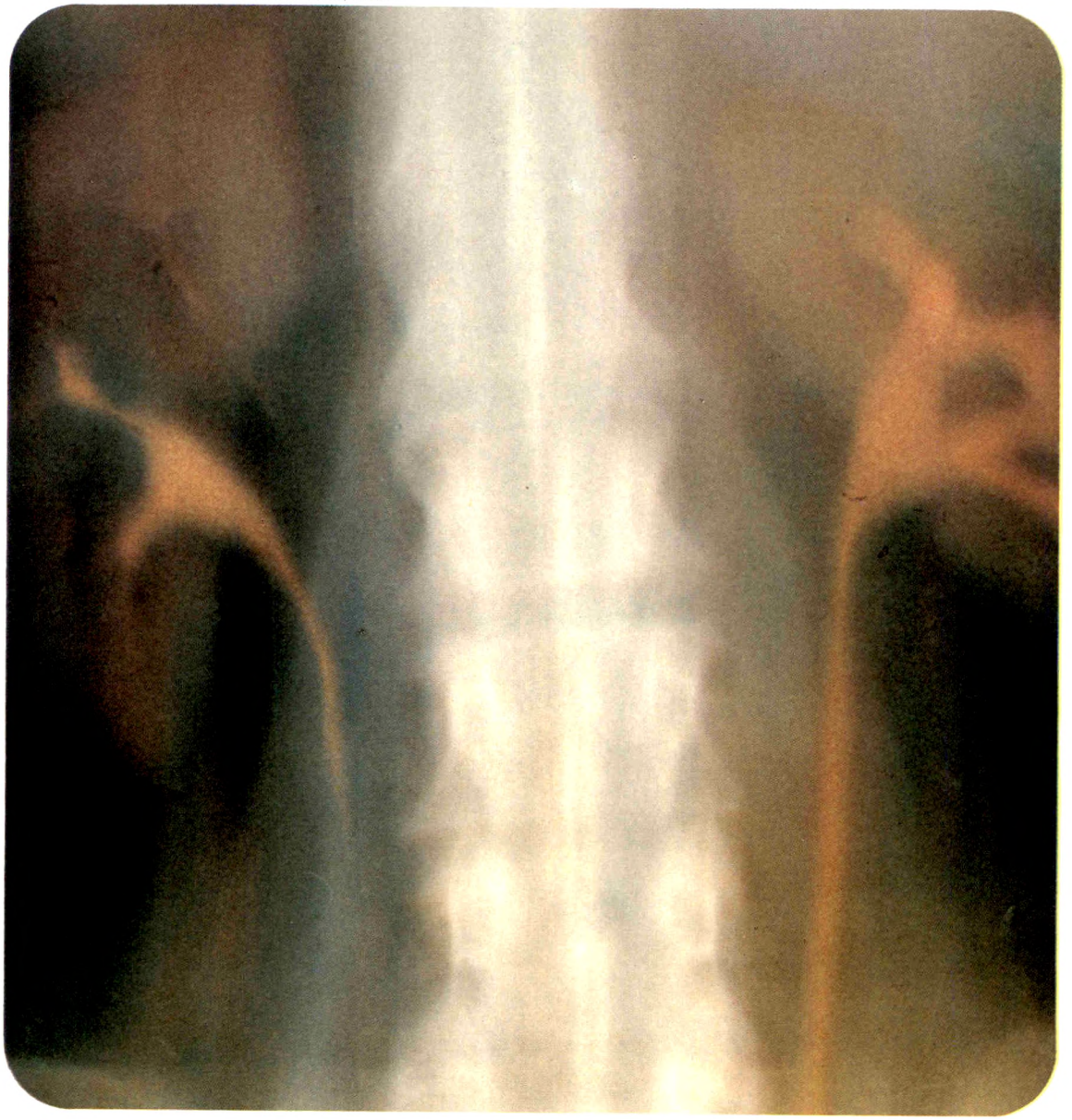
brand of **sodium and meglumine diatrizoates**

Because the cardiac chambers and great blood vessels of the thorax can be effectively visualized with Hypaque-M 75% (90% may be used alternatively), it provides an invaluable aid in the diagnosis of a variety of congenital and acquired cardiac defects. Angiocardiography has also proved useful in the study of neoplastic and infectious diseases of the heart. Hypaque-M 75% used for this purpose is freely miscible with blood, relatively non-irritating and nontoxic in recommended dosage, and is rapidly eliminated by the kidneys.

Nephrotomography

using Hypaque®-M, 90% as the contrast medium*

*Color technique of Robert E. Wise, M.D.



and you'll get the same precise black-and-white definition using

Hypaque®-M, 90%

brand of **sodium and meglumine diatrizoates**

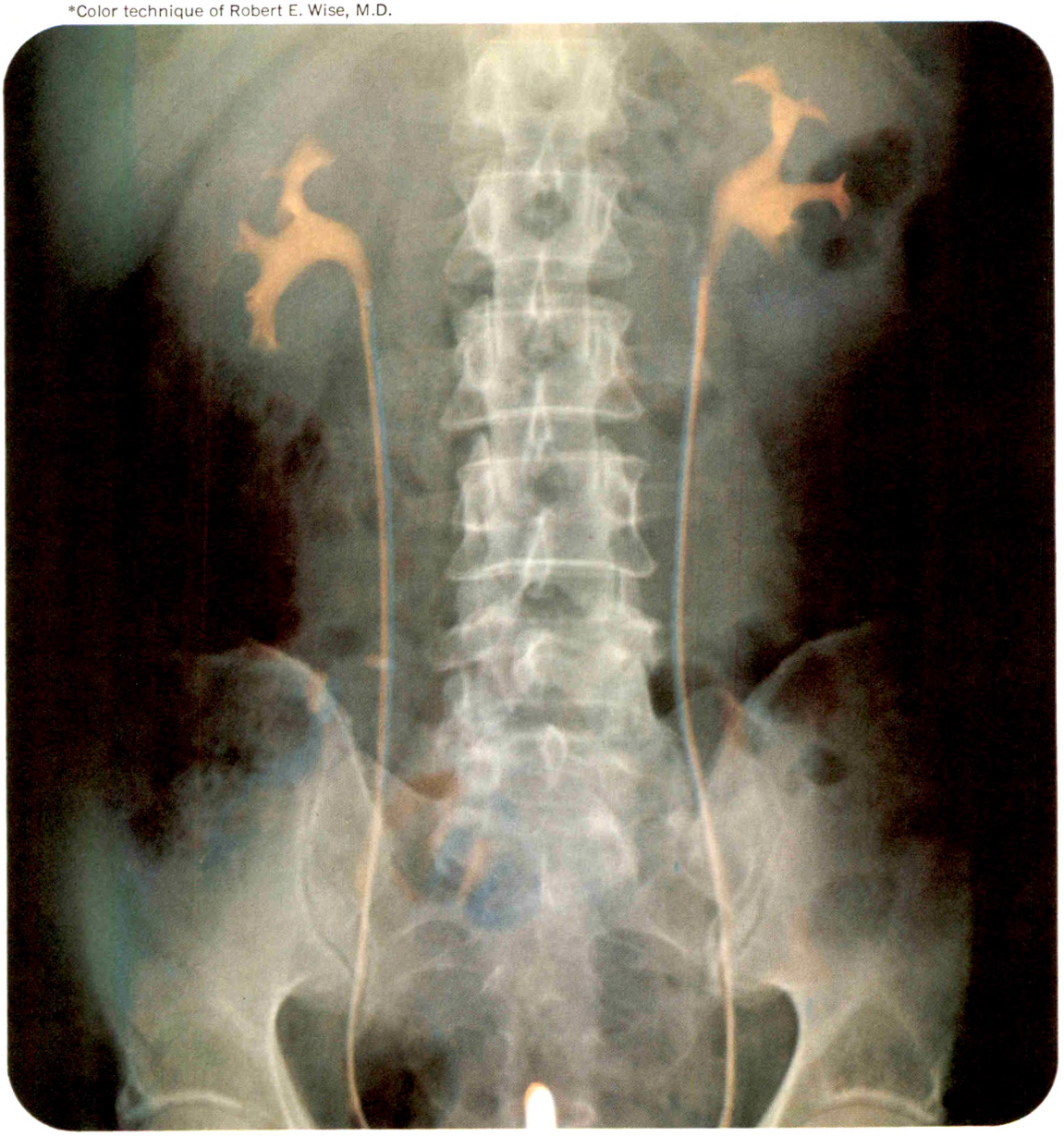
One of the newer methods employed to reveal the nature of renal lesions is nephrotomography —a combination of rapid intravenous nephrography and body-section radiography which provides precise delineation of renal parenchyma. Nephrotomography with Hypaque-M 90% is used primarily to differentiate renal cysts from neoplasms, but may also be indicated to distinguish renal from extrarenal masses and to demonstrate congenital anomalies of the kidney.

Please read the summary of prescribing information on the last page of this ...

Retrograde Pyelography

using Hypaque® sodium 20% as the contrast medium*

*Color technique of Robert E. Wise, M.D.



and you'll get the same precise black-and-white definition using

Hypaque® 20%
sodium
brand of **sodium diatrizoate**

When loss of renal function or other causes result in unsatisfactory delineation of the urinary tract with intravenous techniques, retrograde pyelography with Hypaque sodium 20% solution can provide excellent anatomical details.

Please read the summary of prescribing information on the last pages of this unit.

Unsurpassed
• CONTRAST
• TOLERANCE

Pathology precisely defined
with

Hypaque® sodium 50% and 20%

brand of **sodium diatrizoate**

50%, ampuls of 30 ml., vials of 20, 30 and 50 ml.
20%, bottles of 100 ml.

or with

Hypaque®-M, 75% and 90%

brand of **sodium and meglumine diatrizoates**

75%, vials of 20 and 50 ml.
90%, vials of 20 and 50 ml.

Summary of Full Prescribing Information

Hypaque® Sodium 50%
brand of **sodium diatrizoate, USP**

Sterile Aqueous Injection (Weight/Volume)

Excretory Urography and Drip Infusion Pyelography

Description: Hypaque sodium is sodium 3,5-diacetamido-2,4,6-triiodobenzoate, a radiopaque medium used to delineate internal structures.
Warning: Do not use Hypaque sodium for myelography. Injection of even a small amount into the subarachnoid space may produce convulsions and result in fatality.
General and Specific Precautions: Caution is advised in patients with a history of bronchial asthma, other allergic manifestations, or of sensitivity to iodine; these conditions represent a special risk, though not an absolute contraindication. To avoid or minimize possible allergic reactions, premedication with antihistamines may be considered. Benadryl (diphenhydramine hydrochloride) in the same syringe with Hypaque may result in precipitation. A test dose of contrast medium is not entirely reliable. Severe reactions, including fatalities, have occurred with a test dose as well as with the full diagnostic dose.

Caution is advised in patients with severe cardiovascular disease. In patients with impaired renal function and cardiovascular disease, drip infusion pyelography imposes a sudden osmotic and sodium load which can precipitate congestive heart failure. Contrast media injected into arteries or veins can promote sickling of red cells in susceptible individuals. In patients with reduced renal function, repeat of excretory or retrograde pyelography should be delayed at least 48 hours to avoid temporary suppression of urine. In preparation for excretory urography of patients with multiple myeloma, partial dehydration is not recommended, since this may predispose to the precipitation of myeloma protein in the kidney tubules. When thyroid function studies (PBI and 24-hour radioiodine uptake levels) are indicated, they should be performed *prior* to radiographic studies or several days afterwards, to avoid inaccurate results.

Hypaque sodium 50% should always be injected at body temperature.
General and Specific Adverse Reactions: Adverse reactions, usually of a minor nature, have occurred in 10-14 per cent of patients who have received Hypaque intravenously. Reactions due to *faulty technique* include hematomas and ecchymoses, following extravasation from the vein, and pyrogenic reactions. *Hemodynamic reactions* include vasodilatation with flushing, hypotension and, rarely, vein cramp or thrombophlebitis. Serious *cardiovascular reactions* include rare cases of cardiac arrhythmias (e.g., ventricular fibrillation), shock, and cardiac arrest. Transient proteinuria may occur occasionally following the injection of radiopaques and, rarely, oliguria and anuria have been reported secondary to a hypotensive reaction. *Allergic reactions* include asthmatic attacks, nasal and conjunctival symptoms, cutaneous reactions such as urticaria and, rarely, anaphylactic shock, sometimes with fatal outcome. Severe reactions may also be manifested by signs and symptoms relating to the *respiratory system* (dyspnea, cyanosis, pulmonary or laryngeal edema), or to the *nervous system* (restlessness, confusion, or convulsions). *Other reactions* include nausea, vomiting, excessive salivation, anxiety, headache, and dizziness. Infrequently, "iodism" (salivary gland swelling) from organic compounds appears two days after exposure and subsides by the sixth day. Reactions to drip infusion pyelography may not appear until some hours after the examination.

Angiography

(Peripheral Arteriography and Venography)

Precautions (See also General Precautions): Extreme caution is advised in considering peripheral arteriography in patients suspected of having thromboangiitis obliterans (Buerger's disease). Any procedure (even needling or insertion of a catheter) may induce a severe arterial and/or venous spasm. Caution is also advisable in patients with severe ischemia associated with ascending infection.
Adverse Reactions (See also General Adverse Reactions): In addition to those listed under General Adverse Reactions, are those due to arterial trauma during the procedure (i.e., needling, insertion of catheter, subintimal injection, perforation, etc.) as well as to the hypertonicity or effect of the medium; also reported are transient arterial spasm, extravasation, hemorrhage, hematoma with tamponade, injury to nerves proximal to artery, thrombosis (rare in venography; if vein is irrigated following injection), dissecting aneurysm, arteriovenous fistula, (e.g., with accidental perforation of femoral artery and vein during needling), transient leg pain from contraction of calf muscles in femoral arteriography; transient hypotension after intraarterial (brachial) injection, and brachial plexus injury with axillary artery injections.

Hypaque® Sodium 50% brand of **sodium diatrizoate (cont.)**

Cerebral Angiography: Because of the special techniques required, it is recommended that Hypaque sodium be used for this purpose only by persons skilled and experienced in carrying out this procedure.
Contraindication: Carotid angiography should be avoided during the progressive period of a stroke, since this increases the risk of cerebral complications.
Precautions (See also General Precautions): Select patients for this procedure with care. Use the 50 per cent solution with caution in extreme senility (but not old age, *per se*); advanced arteriosclerosis; severe hypertension; and cardiac decompensation.

The diagnostic value of the procedure, according to many authorities, when employed early enough in locating lesions amenable to surgery, may outweigh the added risk to patients who have recently experienced cerebral embolism or thrombosis (stroke syndrome). A small number of postangiographic fatalities, including progressive thrombosis, have occurred in which the procedure did not appear to play a role.

Patients with severe cerebrovascular disease may be examined primarily by indirect methods of angiography.

Care should be exercised to avoid contaminating catheters, syringes, needles, and contrast media with glove powder or cotton fibers.

Angiography is hazardous in subarachnoid hemorrhage. In migraine, the procedure can be hazardous because of ischemic complications, particularly if performed during or soon after an attack.
Adverse Reactions (See also General Adverse Reactions): The major sources of complications are faulty technique, occlusive atherosclerotic vascular disease, repeated injections of the contrast media, and higher doses than those recommended.

Untoward reactions are mostly mild and transient, although permanent visual field defects and deaths have been reported.

Vascular reactions: flushing, vessel spasm, thrombophlebitis, and cutaneous petechiae.

Neurologic complications: transient cerebral blindness, neuromuscular disorders, convulsions, coma, hemiparesis, unilateral dysesthesias, visual field defects, aphasia, and respiratory difficulties.

Aortography

Precautions (See also General Precautions): Special caution is advised to avoid inadvertent intrathecal injection when using the translumbar technique. The incidence and severity of reactions or complications that may occur are influenced by: the care and experience with which the procedure is performed; the amount and type of medium used; the age and condition of the patient; and the premedication and anesthesia used. Since aortography is not without some danger, it should be performed only by those experienced in the technique. Wherever possible, repeated injections of the solution during a single study should be avoided.
Adverse Reactions (See also General Adverse Reactions): Renal damage and shutdown; neurologic complications such as transverse myelitis or paraplegia; cardiovascular complications such as shock, cardiac arrest or failure, coronary occlusion, arterial thrombosis, embolism, and perforation of vessels; extravasation or hemorrhage from the puncture site or retroperitoneal catheter perforation; necrosis of the intestinal wall; acute pancreatitis; deaths; diffuse cutaneous petechiae; subintimal injection and aortic dissection.
Intraosseus Venography (See General Precautions and Adverse Reactions): A general anesthetic is sometimes necessary since the method is painful. Occasionally, extravasation of the contrast medium from the needle into the soft tissue may occur.

Direct Cholangiography

Precaution (See also General Precautions): This procedure should be used with caution in the presence of acute pancreatitis, injecting no more than 5 to 10 ml. without undue pressure.
Adverse Reactions (See also General Adverse Reactions): These may be attributed to injection pressure or excessive volume of the medium, resulting in overdistention. Such pressure may produce a sensation of epigastric fullness, followed by moderate pain in the back or right upper abdominal quadrant, which will subside when injection is stopped.

Some of the medium may enter the pancreatic duct and cause a transient serum amylase elevation 6 to 18 hours later, without apparent ill effects. Pancholangitis resulting in liver abscess has been reported. Occasionally, nausea, vomiting, fever, and tachycardia have been observed.

Hysterosalpingography

Contraindications: Menstruation, active or imminent; infection in any part of the genital tract, including the external genitalia; pregnancy, known or suspected. Use not advised for six months after end of pregnancy, or 30 days after conization or curettement.

Precaution (See also General Precautions): Caution should be exercised in patients with known or suspected carcinoma to avoid possible spread of the lesion by the procedure.

Splenoportography

Precautions (See also General Precautions): Procedure should be performed with caution on patients with blood dyscrasias, a tendency to severe bleeding, or a spleen recently become tender and palpable.
Adverse Reactions (See also General Adverse Reactions): Persistent hemorrhage with hemoperitoneum has been reported, and, in some instances, hemorrhage has required splenectomy.
How Supplied: Ampuls of 30 ml., boxes of 1, 10, and 25. A 1 ml. sensitivity test ampul is furnished with each ampul. Vials of 20 and 30 ml., rubber stoppered, boxes of 1, 10, and 25. Vials of 50 ml., rubber stoppered, boxes of 1 and 10. Each vial contains sufficient excess to permit withdrawal of 1 ml. for testing sensitivity.

If the solution is chilled, crystals may form but will readily dissolve if the ampul or vial is placed in moderately hot water before use. Cool to body temperature before injecting.

Hypaque® Sodium 20%

brand of **sodium diatrizoate**

Sterile Aqueous Solution 20% (weight/volume)

Precautions: It has long been known that oliguria or anuria may rarely follow bilateral retrograde pyelography or uncomplicated cystoscopic ureteral manipulation. Various mechanisms have been proposed to explain this occurrence, such as reflex anuria, edema, and occlusion of the ureteral orifices from local trauma, pressure, manipulation, sensitivity to the radiopaque medium or to residual disinfecting antiseptic on ureteral catheters, pyelotubular backflow, transient interstitial renal edema with increased pressure, and reduced renal blood flow. Because of the possibility of acute renal failure following bilateral retrograde pyelography, some authors conclude that retrograde pyelography should be done on only one side at a time.
Side Effects: The nonirritating properties of the medium minimize the likelihood of ureteropelvic spasm; in addition, a more natural outline of the upper urinary tract is obtained because of these properties. There is also a decrease in the incidence and severity of discomfort and colic following retrograde examination. Excellent tolerance was evidenced by notably few untoward reactions. Minor side reactions, which occurred in a few patients, consisted of nausea, vomiting, excessive salivation, and sweating. There was no indication of irritation of the urinary tract mucosa that could be attributed to the medium.

With Hypaque Sodium 20 per cent, reflux into the blood stream or lymphatics (pyelovenous or pyelolymphatic backflow) as a result of undue pressure of administration is not apt to result in a generalized reaction, since intravenous injection of more than double this concentration has been well tolerated.

Hypaque®-M, 75%

brand of **sodium and meglumine diatrizoates**

Sterile Aqueous Injection 75% (weight/volume)

Caution: The 75 per cent concentration is intended primarily for angiocardiography, nephrotomography and selected cases of peripheral angiography. Hypaque sodium (brand of diatrizoate sodium) 50 per cent solution is recommended for excretory urography, cerebral angiography and most cases of peripheral angiography.
Warning: Do not use Hypaque-M, 75 per cent for myelography. Injection of even a small amount into the subarachnoid space may produce convulsions and result in fatality.

Angiocardiography

Contraindications: Use of Hypaque-M, 75 per cent is contraindicated in patients with advanced renal destruction associated with severe uremia. Hypaque-M 75 per cent should not be used for myelography.
Precautions: 1. Caution is advised in patients with hyperthyroidism, hypertension, active tuberculosis and a history of allergy, especially to iodine. Angiocardiography and nephrotomography should be performed cautiously in patients with heart disease and circulatory failure and should not be employed in patients who are in collapse or who are critically ill or debilitated. A renal function test is advisable before administration of the 75 per cent solution.

2. Prior to the examination, the patient may be tested for sensitivity to the radiopaque medium. (See Side Effects and Sensitivity Tests.) Patients who show an idiosyncrasy should not be given the drug.

3. Premedication with a barbiturate is advisable if the patient is extremely nervous. Demerol (brand of meperidine), chlorpromazine and antihistamines have also been recommended for premedication. Such antihistamines as chlorpheniramine maleate or tripelennamine hydrochloride may be administered about 30 minutes before injection of the radiopaque medium or may be combined with it in a single injection. Many authorities recommend general anesthesia for small children and uncooperative patients.

4. Facilities for resuscitation including a mask with a breathing bag and pure oxygen should be available for immediate administration in case of severe reaction.

5. The sensations to be experienced should be described to the patient in order to allay apprehension before injection and to prevent excitement afterward.

6. To facilitate venipuncture, the needle should be sharp, the arm extended and the vein large and fully distended.

7. The syringe must be scrupulously clean in order to prevent sticking of the plunger during injection.

8. If crystals form, the solution should be warmed and agitated until they have redissolved. Injection should be made only when the solution is clear and is at a temperature of approximately 37.5° C.

9. Injection should be made only when there is free communication between needle and vein. When in doubt, another vein should be tried or the test postponed. Vein and needle should be watched during injection to prevent displacement of the needle or overdistention of the vein. If extravasation occurs, the injection should be stopped and a quantity of physiologic saline solution administered through the needle to dilute the radiopaque medium and to lessen the possibility of irritation.

10. Some authorities advise that repeated injections should not be given in close sequence and, if possible, should be avoided.

Side Effects and Sensitivity Tests: As with other radiopaque mediums, certain side effects occasionally may be encountered, although the 75 per cent solution has been well tolerated when given in recommended dosages. Serious complications following angiocardiography may be due to varying and perhaps unrelated factors. Symptoms may be due to the speed of injection and the anxiety and psychic stress associated with the examination, as well as to the material injected. Side effects will usually be minor and transient and may include a sensation of warmth and flushing, nausea, vein cramp, mild tachycardia, metallic or acid taste, tightness in the chest, headache, cough or urticaria. Delayed reactions may occur. Venous thrombosis has not been observed in patients receiving the 75 per cent solution, but as with any rapidly injected hypertonic solution, the possibility of this complication exists.

Angiocardiographic contrast mediums may produce symptoms of an anaphylactic nature in sensitive persons. Patients should be observed carefully during injection, as serious reactions including fatalities have occurred with most mediums. Since it is believed that reactions to intravenously administered organic iodine radiopaque agents are more likely to develop in patients with allergic diathesis, special care is advisable in persons with a history of asthma or other allergic manifestations.

Various methods have been advocated to detect sensitivity to contrast mediums, particularly conjunctival, oral, intradermal and intravenous testing. Conjunctival, oral and intradermal tests are not reliable, since reactions to them are generally caused by direct local vascular effect. Occasionally a severe reaction in the eye has followed a conjunctival test. An intravenous test is more likely to demonstrate sensitivity, although a negative reaction does not necessarily rule out the possibility. A small dose of 0.5 to 1 ml. is slowly injected intravenously over a period of one minute, followed by a period of observation sufficiently long to detect delayed reactions. Although allergic reactions generally occur quickly, occasionally they may not be manifested for 10 or even 15 minutes.

Warning signs and symptoms of possible intolerance or allergy include respiratory difficulty (wheezing, dyspnea or sensation of suffocation or tightness in the throat or chest), sneezing, itching, urticaria, nausea or vomiting and fainting.
Treatment of Reactions: (Same as with Hypaque Sodium 50%)

Nephrotomography

Contraindications, Precautions, Side Effects and Treatment of Reactions: See Angiocardiography.

Hypaque®-M, 90%

brand of **sodium and meglumine diatrizoates**

Sterile Aqueous Injection 90% (weight/volume)

Caution: Hypaque-M, 90 per cent is intended primarily for angiocardiography, nephrotomography, hysterosalpingography and selected cases of peripheral angiography. Hypaque sodium

Hypaque®-M, 90%
brand of **sodium and meglumine diatrizoates (cont.)**

50 per cent solution is recommended for excretory urography, cerebral angiography and most cases of peripheral angiography. *Warning:* Do not use Hypaque-M, 90 per cent for myelography. Injection of even a small amount into the subarachnoid space may produce convulsions and result in fatality.

Angiocardiography

Contraindications: Use of Hypaque-M, 90 per cent is contraindicated in patients with advanced renal destruction associated with severe uremia. Hypaque-M, 90 per cent should not be used for myelography.

Precautions: 1. Caution is advised in patients with hyperthyroidism, hypertension, active tuberculosis and a history of allergy, especially to iodine. Angiocardiography and nephrotomography should be performed cautiously in patients with heart disease and circulatory failure and should not be employed in patients who are in collapse or who are critically ill or debilitated. A renal function test is advisable before administration of Hypaque-M, 90 per cent.

2. Prior to the examination, the patient may be tested for sensitivity to Hypaque-M, 90 per cent. (See Side Effects and Sensitivity Tests.) Patients who show an idiosyncrasy to Hypaque-M, 90 per cent should not be given the drug.

3. Premedication with a barbiturate is advisable if the patient is extremely nervous. Demerol (brand of meperidine), chlorpromazine and antihistamines have also been recommended for premedication. Such antihistamines as chlorpheniramine maleate or tripelennamine hydrochloride may be administered about thirty minutes before injection of Hypaque-M, 90 per cent or may be combined with it in a single injection. Many authorities recommend general anesthesia for small children and uncooperative patients.

4. Facilities for resuscitation including a mask with a breathing bag and pure oxygen should be available for immediate administration in case of severe reaction.

5. The sensations to be experienced should be described to the patient in order to allay apprehension before injection and to prevent excitement afterward.

6. To facilitate venipuncture, the needle should be sharp, the arm extended and the vein large and fully distended.

7. The syringe must be scrupulously clean in order to prevent sticking of the plunger during injection.

8. Hypaque-M, 90 per cent should be warmed and agitated until all suspended crystals have redissolved. Injection should be made only when the solution is clear and is at a temperature of approximately 37.5°C.

9. Injection should be made only when there is free communication between needle and vein. When in doubt, another vein should be tried or the test postponed. Vein and needle should be watched during injection to prevent displacement of the needle or overdistention of the vein. If extravasation occurs, the injection should be stopped and a quantity of physiologic saline solution administered through the needle to dilute the Hypaque-M, 90 per cent and to lessen the possibility of irritation.

10. Some authorities advise that repeated injections should not be given in close sequence and, if possible, should be avoided.

Hypaque®-M, 90%
brand of **sodium and meglumine diatrizoates (cont.)**

Side Effects and Sensitivity Tests: Serious complications following angiocardiography may be due to varying and perhaps unrelated factors. Symptoms may be due to the speed of injection and the anxiety and psychic stress associated with the examination, as well as to the material injected. Side effects noted with Hypaque-M, 90 per cent were usually of a minor and transient nature and included a sensation of flushing or warmth, nausea, vein cramp, mild tachycardia, metallic or acid taste, tightness in the chest, headache, cough or urticaria. Delayed reactions may occur. Venous thrombosis has been observed in patients following the percutaneous insertion of the injection needle. This complication may be anticipated, however, when concentrated hypertonic solutions are injected rapidly. In skilled hands, the administration of Hypaque-M, 90 per cent is attended by comparatively few untoward reactions.

Angiocardiographic contrast mediums may produce symptoms of an anaphylactic nature in sensitive persons. Patients should be observed carefully during injection, as serious reactions including fatalities have occurred with most mediums. Since it is believed that reactions to intravenously administered organic iodine radiopaque agents are more likely to develop in patients with allergic diathesis, special care is advisable in persons with a history of asthma or other allergic manifestations.

Various methods have been advocated to detect sensitivity to contrast mediums, particularly conjunctival, oral, intradermal and intravenous testing. Conjunctival, oral and intradermal tests are not reliable, since reactions to them are generally caused by a direct local vascular effect. Occasionally a severe reaction in the eye has followed a conjunctival test. An intravenous test is more likely to demonstrate sensitivity, although a negative reaction does not necessarily rule out the possibility. A small dose of from 0.5 to 1 ml. is slowly injected intravenously over a period of one minute, followed by a period of observation sufficiently long to detect delayed reactions. Although allergic reactions generally occur quickly, occasionally they may not be manifested for ten or even fifteen minutes.

Warning signs and symptoms of possible intolerance or allergy include respiratory difficulty (wheezing, dyspnea or sensation of suffocation or tightness in the throat or chest), sneezing, itching, urticaria, nausea or vomiting and fainting. *Treatment of Reactions:* (Same as with Hypaque Sodium 50%)

Nephrotomography

Contraindications, Precautions, Side Effects and Treatment of Reactions: See Angiocardiography.

Hysterosalpingography

Contraindications: The procedure should not be performed during the menstrual period or when menstrual flow is imminent, nor should it be performed when infection is present in any portion of the genital tract, including the external genitalia. The procedure is also contraindicated for pregnant women or for those in whom pregnancy is suspected. Its use is not advised for six months after termination of pregnancy, or for thirty days after conization or curettement.

Precautions: In patients with carcinoma or in those in whom the condition is suspected, caution should be exercised to avoid possible spread of the lesion by the procedure.

For more detailed information on these products, please read the package circulars.

Pathology Precisely Defined

Hypaque® Sodium 20% and 50%
brand of **sodium diatrizoate**

Hypaque® M, 75% and 90%
brand of **sodium and meglumine diatrizoates**

Winthrop **PIONEERS IN PRODUCTS FOR RADIOLOGIC DIAGNOSIS**

PRINTED IN U.S.A. ISSUED JAN. 1969 (1326

THE AMERICAN JOURNAL OF ROENTGENOLOGY
RADIUM THERAPY AND NUCLEAR MEDICINE

VOL. 105 APRIL, 1969 No. 4

FLUORESCENT THYROID SCANNING*

By PAUL B. HOFFER, M.D.†
CHICAGO, ILLINOIS

A TECHNIQUE has been devised for the detection and mapping of the stable I^{127} within the thyroid gland. No radioactive isotope is introduced into the patient. A solid state, lithium-drifted silicon crystal is used to detect fluorescent radiation stimulated in the patient's thyroid gland.[4]

A model unit has been designed which operates as an "accessory" mounted on a conventional rectilinear scanner and uses the scanner's amplifier, pulse height analyzer and read-out system.

Conventional roentgenographic techniques are insufficiently sensitive to demonstrate the low absolute concentration of iodine within the thyroid gland (0.04 per cent by weight).[9] Jacobson,[6] Edholm and Jacobson,[2] MacKay,[8] Heedman and Jacobson,[3] and Roy *et al.*[12] have utilized the principles of dichromography to demonstrate such low iodine concentrations. Unfortunately, these systems are so sophisticated that they are impractical outside the experimental laboratory.

The development of the "solid state" detector, with its excellent energy resolution characteristics, has made fluorescent chemical analysis feasible. The system to be described incorporates the concept of fluorescent spectroscopy into a practical biologic scanning system for low concentrations of iodine or other high atomic number elements.

MATERIAL AND METHOD

An encapsulated pellet of americium 241 is used as a source of low energy monochromatic gamma rays (for each 100 alpha disintegrations, americium 241 emits 36 gamma rays at 59.57 kev. and smaller numbers of gamma and x-rays at energies below 26.36 kev. All of the alpha particles are either self-absorbed or absorbed in the encapsulating material).[5] The americium 241 source is placed in the midplane and to one side of the lead collimator block. In the center of the same block is a 4.1 cm. tapered bore vertical hole. Above this hole is a 30 $mm.^2$ lithium-drifted silicon detector in a low temperature vacuum housing (modified TMC Model 334). Both the detector and the source are focused at the same point 2 cm. below the collimator

* Presented at the Sixteenth Annual Meeting of the Association of University Radiologists, Columbus, Ohio, May 8–11, 1968.
From the Department of Radiology, University of Chicago, Chicago, Illinois.
† Assistant Resident in Radiology: Winner of Memorial Medal Award of the Association of University Radiologists, 1968.

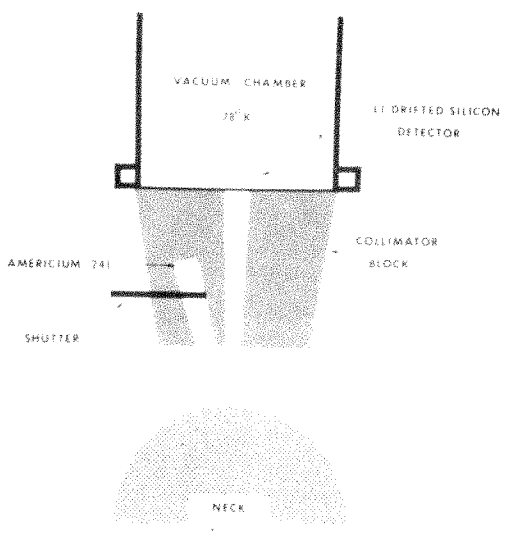


FIG. 1. Schematic representation of the source-detector section of the fluorescent scanner.

block (Fig. 1). In the actual working model, focusing is compromised to allow a 3 cm. depth of focus in which source and detector collimation overlap.

The entire source, detector, and collimator system is mounted on a rectilinear scanner (Picker Magnascanner). With the patient's neck beneath the collimator, the thyroid gland is scanned as for a conventional thyroid scan (Fig. 2).

When the 59.57 kev. gamma ray from the americium 241 source interacts with a K-shell electron of an iodine atom within the thyroid gland, a photoelectron is produced and a vacancy is created in the K-shell. Filling of this vacancy by an electron from one of the outer shells leads to production of characteristic x rays. The fluorescence yield is 87 per cent, the remaining 13 per cent of interactions leading to the creation of an Auger electron. Eighty-eight per cent of the characteristic x rays produced will be K_α x rays with an almost uniform energy of 28.5 kev. (the remainder of the x rays produced will be K_β with a mean energy of 32.3 kev.).[1] The K_α characteristic x ray of iodine has a half-value layer in soft tissue of approximately 2 cm.

If these K_α x rays are produced in the region where the source and detector collimators overlap, a certain fixed percentage will be "seen" by the solid state

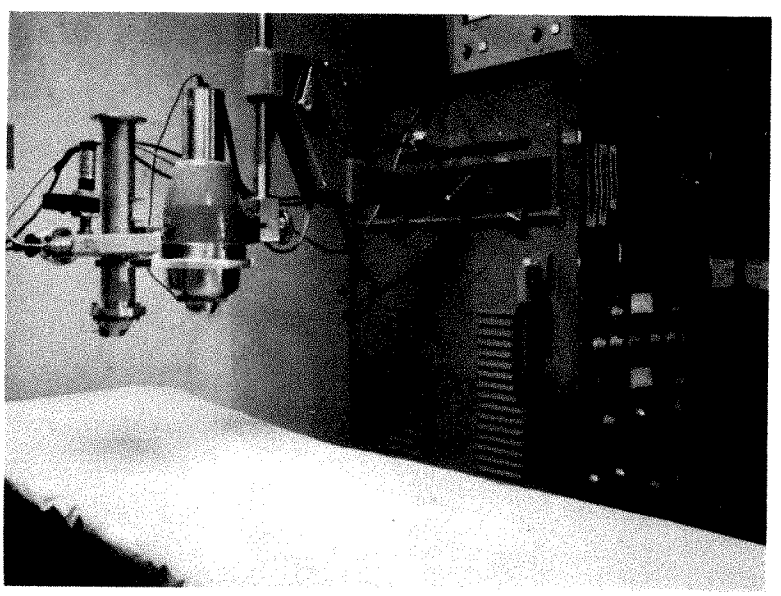


FIG. 2. Photograph of the fluorescent scanning assembly. The fluorescent scanner is mounted on the front of the 3 inch crystal housing of a Picker Magnascanner. The 3 inch NaI crystal and photomultiplier tube are electronically disconnected during fluorescent scanning. The fluorescent scanner (modified TMC Model 334) can be detached when not in use.

detector. The energy resolution of the lithium-drifted silicon detector is less than 500 ev. full width at one-half maximum at 28.5 kev. If, therefore, a narrow window of about 1 kev. is set on the pulse height analyzer system between 28 and 29 kev., a high percentage of the K_α characteristic x rays will be recorded and the "noise," due primarily to multiple Compton interactions, will be minimized. In practice, a 3 to 1 signal to noise ratio has been counted over the center of normal thyroid lobes. Figures 3 and 4 show a photograph and a scan of a normal thyroid gland phantom.

The efficiency of production of K_α x rays with this method is poor. Only a minute percentage of the incident gamma rays interacts with an iodine atom inside the thyroid gland. Even when such an event occurs, the vast majority of K_α x rays produced are "lost" to the view of the detector due to its small size. During scanning, however, only the area of interest, *i.e.*, the area within the view of the crystal, is irradiated. For example, in a 1 hour scan, a single region within the gland may only be irradiated for a period of 1 minute or less.

The prototype scanner currently in use has a weak americium source of 300 mc. During the phantom scan shown in Figure 4, the thyroid gland received a radiation dose of 75 millirads. In the first human study done with the prototype scanner, a fair quality scan was obtained with a dose of approximately 50 millirads to the patient's thyroid gland (dosimetry measurements were made using a Victoreen ionization chamber surrounded by bolus). Although ideal count densities for this type of scanning have not yet been established, it can be safely predicted that scans of good quality will not require a dose of more than 500 millirads to the thyroid gland, and can probably be successfully accomplished in the 100 to 200 millirad range. This dose is substantially less than that received in an iodine 125 or iodine 131 scanning,[13] and compares favorably with the dose received by the thyroid gland in a stereoscopic cervical spine study by conventional roentgenography.[7]



Fig. 3. A 12.5 gm. human thyroid gland embedded in a plastic phantom. The cracks seen here are in the lucite mold. The minimum gland surface to phantom surface thickness is 3 mm.

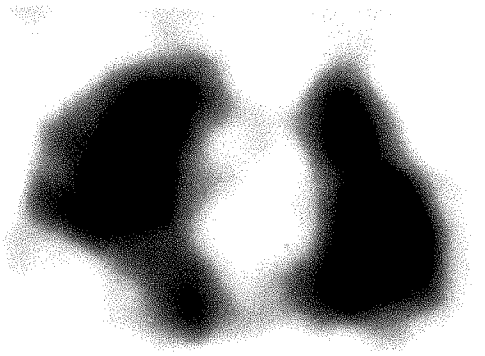


Fig. 4. Fluorescent scan of the thyroid gland seen in Figure 3. The radiation dose to the phantom was 75 millirads. (A gaussian spot projector was used to form the image.)

RESULTS

During our preliminary studies we have had the opportunity of examining a patient with a palpable nodule in the middle of the left lobe of the thyroid gland. A technetium 99m pertechnetate thyroid scanning was done 6 hours prior to the fluorescent scanning and revealed no uptake in the region of the nodule (Fig. 5*A*). A flushing dose of perchlorate was given to the patient immediately following the pertechnetate scanning to clear the technetium 99m from the gland. Prior to the fluorescent

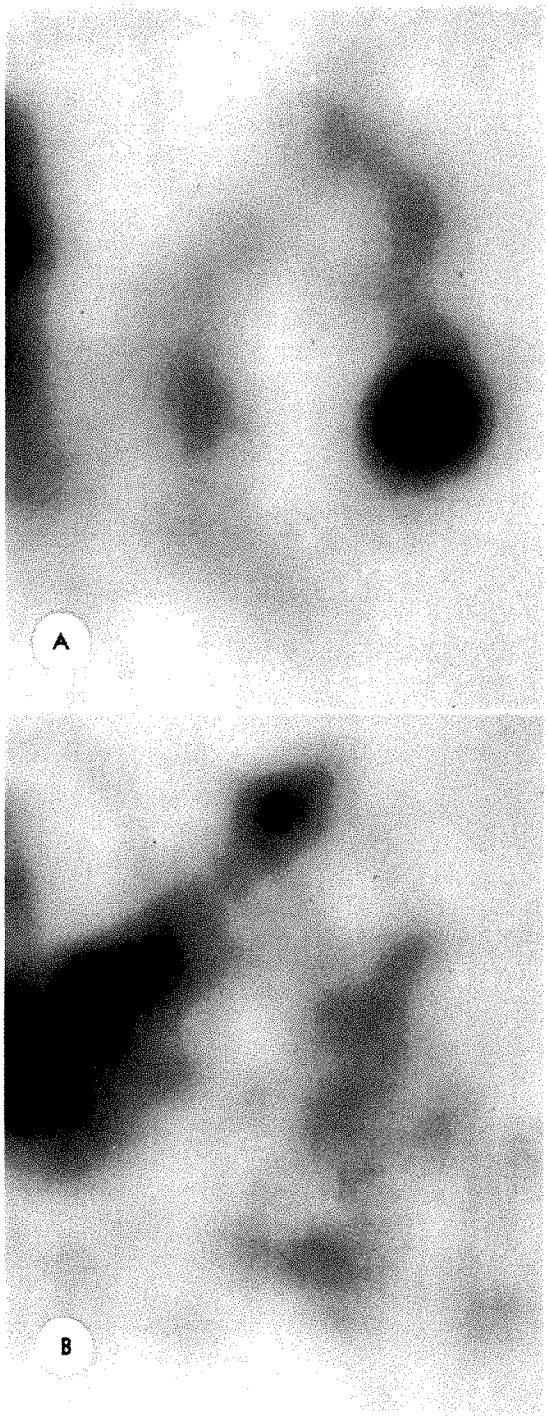


FIG. 5. (*A*) Technetium 99m pertechnetate scan of a patient with a large, palpable nodule in the center of the left lobe of the thyroid gland. The entire left lobe and medial aspect of the right lobe are shown. The nodule corresponded in location to the "cold" area in the center of the lobe. The small "hot" spot adjacent to the nodule is unexplained. (*B*) Fluorescent scan of the region shown in *A*. In spite of the lack of detail (due to low source strength), a "cold" area is seen in the center of the lobe.

scanning, background counts were made over the right lobe of the thyroid gland, over an adjacent region of the neck, and over the dorsal surface of the patient's left hand to quantify residual background. These counts were made with the shutter of the americium 241 source closed. A background rate of approximately 12 counts per minute was recorded in each area, indicating no selective interference in the thyroid region from the prior technetium 99m pertechnetate study. A 50 minute scanning was done using a 300 mc americium 241 source. The examination was restricted to the left lobe of the gland because of the long scanning time required (due to the low strength of the americium 241 source used in this prototype set-up). The scan (Fig. 5*B*) revealed low iodine concentration in the region of the nodule. At surgery the entire left lobe of the thyroid gland was excised and a fluid-filled cyst was demonstrated (Fig. 6).

DISCUSSION

Conventional thyroid scanning techniques give direct information concerning the distribution of metabolic activity (as determined by iodine uptake) within the



FIG. 6. Pathologic specimen of left lobe of thyroid gland shown in Figure 5. This photograph was taken following sectioning of the fluid filled serous cyst in the center of the lobe.

thyroid gland. The fluorescent scan gives information about the distribution of iodine within the gland *regardless* of its organic state or metabolic potential. The *combination* of these two techniques should give a more *complete* picture of thyroid pathology. The work of Medeiros-Neto *et al.*[10] suggests that certain areas of metabolic inactivity (*i.e.*, "cold" nodules) within the thyroid gland contain significant amounts of iodine in the form of normal and abnormal iodoproteins.[11] The ability of the fluorescent scan to determine the iodine content of these nodules may eventually aid in their differential diagnosis.

Our collimator system is currently being modified to accommodate a 3 to 5 curie americium 241 source. This will allow scanning of the entire thyroid gland in less than 30 minutes, a reasonable scanning time. The relation of source strength to duration of examination is the same in fluorescent radiography as it is in conventional radiography, *i.e.*, radiation dose is proportional to photon flux×time. A higher activity source therefore permits decrease in exposure time without necessarily increasing irradiation of the thyroid gland.

Our current studies have been primarily concerned with the demonstration of I^{127} within the thyroid gland. However, the ability to detect small concentrations of high atomic number elements within living systems has further applications. It is possible to introduce *nonradioactive* tracer materials into the body and record their distribution. To demonstrate, a mouse was injected intravenously with 0.05 cc. of cholographin (methylglucamine iodipamide, 26 per cent iodine). A fluorescent scan for iodine was made between 1 and 2

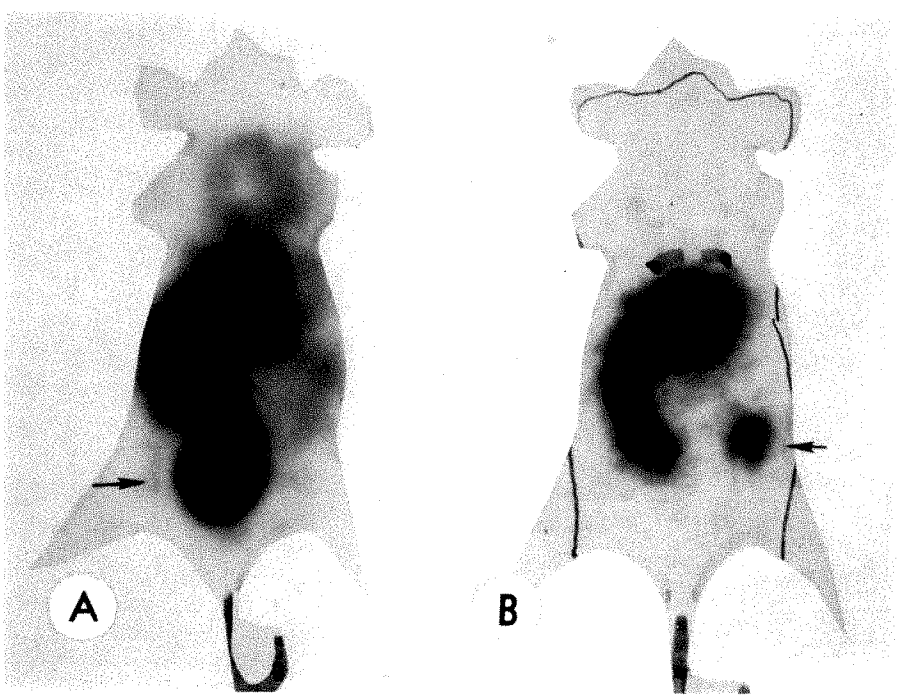


Fig. 7. (*A*) Fluorescent scan for iodine made 1 to 2 hours following the intravenous injection of 0.05 cc. of cholographin (26 per cent iodine) into a mouse. A high concentration of iodine is present in the right upper quadrant of the abdomen as well as the bladder (arrow). (*B*) Conventional isotope scan made approximately 1 hour following the intravenous injection of 50 μc I^{131} labeled rose bengal into the same mouse. The distribution of the activity in the right upper quadrant of the abdomen resembles the fluorescent scan. The diaphragm is marked for orientation (the arrow points to activity in the colon following a previous smaller test dose of I^{131} rose bengal).

hours following injection (Fig. 7*A*). Cholographin is taken up by the parenchymal cells of the liver and excreted via the biliary system. A variable quantity is also excreted by the kidneys. Iodine is demonstrated in the right upper quadrant of the abdomen in a pattern suggesting liver, gallbladder, and duodenum. The urinary bladder is also seen. In order to confirm these results, the same animal was later injected with 50 μc I^{131} labeled rose bengal and a conventional isotope scan using NaI crystal was obtained. (The biliary excretion of I^{131} rose bengal is similar to that of cholographin.) The activity in the right upper quadrant following the rose bengal injection (Fig. 7*B*) closely resembles the distribution of iodine seen following the cholographin fluorescent scan.

In fluorescent scanning, the area "seen" is defined by the intersection of two "paths," the stimulating photon beam from the radiation source, and the field of view of the detector. Only the volume of material intersected by both paths is recorded. In fluorescent thyroid scanning, an effort is made to maximize this overlap. However, by moving the source away from the subject, collimating it more restrictively, and creating a greater angle between stimulating photon beam and detector field of view, a relatively small area of intersection can be defined. If both source and detector are then scanned in a rectilinear manner, a single plane image or laminogram is produced. By the use of multiple detectors or with a single detector set at varying heights above the subject, multiple laminographic sections may be obtained.

To demonstrate this, a ping-pong ball was filled with 4 per cent nonradioactive

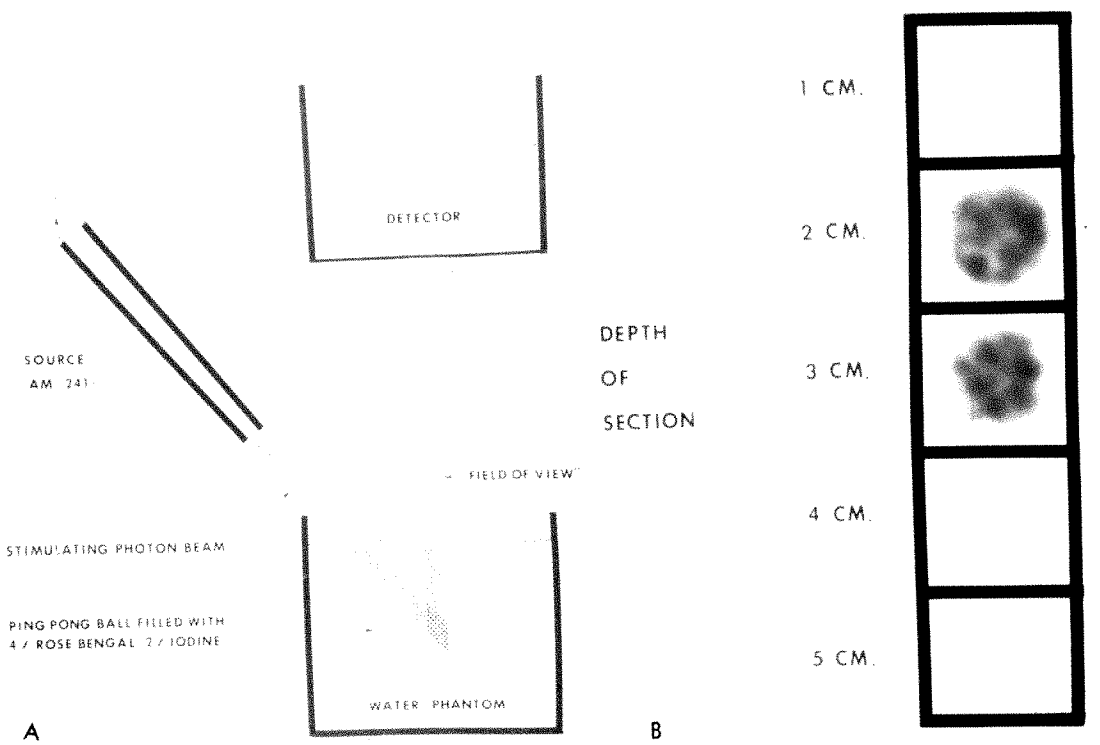


Fig. 8. (*A*) Schematic representation of the system used to produce laminographic fluorescent scans. (*B*) Results obtained following fluorescent laminographic scanning of the phantom described in *A*. The centimeter markers refer to the distance of each laminographic section below the surface of the water. The ping-pong ball is demonstrated in 2, 3 and 4 cm. sections.

rose bengal (approximately 2 per cent iodine), and placed in a water phantom. The stimulating photon beam was adjusted to intersect the detector field of view at a "point" 5 cm. below the surface of the detector collimator face (Fig. 8*A*). The entire source-detector system was then moved down toward the phantom in five 1 cm. steps. At each 1 cm. step a rectilinear fluorescent scan was made. The laminograms obtained demonstrate the ping-pong ball between the 2 and 4 cm. levels (Fig. 8*B*).

It may be practical, in the future, to demonstrate inert "tracers" in other organs. Higher energy sources and lithium-drifted germanium detectors would be useful for such studies and are currently available.

CONCLUSION

A system has been developed for the demonstration of *in vivo* stable I^{127} within the thyroid gland. This system has the following desirable characteristics:

1. No radioactive isotope is administered to the patient.
2. The radiation dose to the thyroid gland is low (less than 500 millirads).
3. The system visualizes all iodine within the gland regardless of the metabolic status of the region in which it is located. For example, when used in conjunction with conventional scanning, fluorescent scanning can delineate the iodine content of "cold" nodules. Hopefully, in some cases, this will permit etiologic identification of such lesions.
4. The unit may be conveniently used in conjunction with the electronics of commonly available rectilinear scanners.

The clinical usefulness of this system is promising, but awaits further investigation.

In addition, preliminary information is presented demonstrating the use of fluorescent scanning for laminographic applications and imaging nonradioactive tracers *in vivo*.

Department of Radiology
University of Chicago
School of Medicine
950 East 59th Street
Chicago, Illinois 60637

REFERENCES

1. CLARK, G. L. The Encyclopedia of X-rays and Gamma Rays. Reinhold, New York, 1963, pp. 1124–1129.
2. EDHOLM, P., and JACOBSON, B. Quantitative determination of iodine *in vivo*. *Acta radiol.*, 1959, *52*, 337–346.
3. HEEDMAN, P., and JACOBSON, B. Thyroid iodine determined by x-ray spectrophotometry. *J. Clin. Endocrinol. & Metabol.*, 1964, *24*, 246–252.
4. HOFFER, P. B., JONES, W. B., CRAWFORD, R. B., BECK, R. N., and GOTTSCHALK, A. Fluorescent thyroid scanning: new method of imaging thyroid. *Radiology*, 1968, *90*, 342–344.
5. HYDE, K. H., BOWMAN, H. R., and SISSON, D. H. Analytical capabilities of semi-conductor x-ray emission spectrometer. UCRL Report 16845, 1966.
6. JACOBSON, B. Dichromatic absorption radiography: dichromography. *Acta radiol.*, 1953, *39*, 437–452.
7. JOHNS, H. E. The Physics of Radiology. Second edition. Charles C Thomas, Publisher, Springfield, Ill., 1961, p. 611.
8. MACKAY, R. S. X-ray visualization and analysis using spectral information. I.R.E. Transactions on Medical Electronics, 1960, ME-7, 77–79.
9. MCGAVACK, T. H. The Thyroid. C. V. Mosby Company, St. Louis, 1951, p. 53.
10. MEDEIROS-NETO, G. A., NICOLAU, W., KIEFFER, J., and PIERONI, R. R. Insoluble iodoprotein in thyroid nodules. In: Current Topics in Thyroid Research. Edited by C. Cassano and M. Andreoli. Academic Press, Inc., New York, 1965, pp. 910–919.
11. PITT-RIVERS, R. V., and TATA, J. R. The Chemistry of Thyroid Diseases. Charles C Thomas, Publisher, Springfield, Ill., 1960, pp. 54–66.
12. ROY, O. L., BEIQUE, R. A., and D'OMBRAIN, G. L. Method of iodine determination by characteristic x-ray absorption. I.R.E. Transactions on Bio-Medical Electronics, 1962, ME-9, 50–53.
13. SMITH, E. M., BROWNELL, G. L., and ELLETT, W. H. Radiation dosimetry. In: Principles of Nuclear Medicine. Edited by H. N. Wagner, Jr. W. B. Saunders Company, Philadelphia, 1968, pp. 742–776.

SERIAL BRAIN SCANNING WITH TECHNETIUM 99m PERTECHNETATE IN CEREBRAL INFARCTION*

By MICHAEL S. USHER, M.D., F.R.C.P.(C),† *and* JAMES L. QUINN, III, M.D.‡
CHICAGO, ILLINOIS

THE radioisotope brain scanning has been established as a reliable, accurate aid in locating brain tumors. It has also been noted that intracerebral abscess, subdural hematoma, and cerebral infarction concentrate radiopharmaceuticals.[6]

The introduction of short-lived radionuclides, such as technetium 99m, has made possible serial brain scanning without excessive irradiation.[4] It has been well documented that the peak incidence of positive brain scans using mercury 197 chlormerodrin[9] or technetium 99m pertechnetate[5] occurs from 1 to 8 weeks after cerebral infarction. However, little information is available in the literature regarding the relationship between the size, density, or changing pattern of isotope distribution and the patient's clinical course.

This study was carried out to reconfirm the temporal variation of positive scans, and to examine the implication of these changes in the severity and the prognosis of the disease.

MATERIAL AND METHODS

The case reports of all patients who had serial brain scan studies between July, 1966 and December, 1967, with at least 1 positive scan, were reviewed. Twenty-eight cases who had cerebrovascular accidents proven clinically, roentgenographically or at necropsy were included. The onset of symptoms, clinical course, condition of the patient at the time of discharge, and follow-up were noted. Patients were followed for at least 2 months, by which time their clinical course had stabilized. Four-view photo scans were made with conventional 3 inch crystal rectilinear scanners immediately after the intravenous injection of 10 to 20 mc of technetium 99m pertechnetate.

Table I

LIST OF CRITERIA USED IN EVALUATION OF THE CLINICAL STATUS OF THE ILLNESS

1.	Transient ischemic attack
2.	Aphasia—incomplete Monoparesis or hemiparesis Partial blindness
3.	Complete aphasia Hemiplegia Complete visual field loss Marked aphasia and marked hemiparesis
4.	Altered consciousness

Two hundred and fifty milligrams of potassium perchlorate was administered by mouth immediately before the injection to reduce salivary gland, thyroid and choroid plexus concentration.

Areas of abnormal radioisotope uptake were measured by planimetry in the lateral projection and their density rated I to IV: I, barely perceptible; II, distinctly seen; III, equal to the vertex; and IV, greater than the vertex.

The patient's clinical status at the onset of the acute episode was rated 1 to 4 by the criteria listed in Table I.

RESULTS

The results of the study are summarized in Table II. There were 31 lesions in 28 patients, 3 patients having 2 lesions each. Twenty-two of these abnormalities appeared on the left side, the remaining 9 on the right. In 2 patients the infarctions were

* Presented at the Sixteenth Annual Meeting of the Association of University Radiologists, Columbus, Ohio, May 8–11, 1968.
From the Department of Radiology, Northwestern University and the Chicago Wesley Memorial Hospital, Chicago, Illinois.
† Associate in Radiology and Associate Director of Nuclear Medicine.
‡ Professor of Radiology and Director of Nuclear Medicine.

embolic in origin. These were demonstrated by increased uptake in the left frontal and left occipital region in 1 case, and the left frontal region in the other.

The most common location of infarction was about the sylvian fissure, the posterior limits of middle cerebral arterial flow.

Time-Density Relationship. Figure 1 demonstrates the time-density relationship in patients who recovered completely. The earliest positive scan in this series occurred at Day 4 in a patient with transient aphasia. The latest initial negative scan was observed at Day 6. Scans made after 2 weeks tended to become less dense.

Figure 2 shows the time-density relationship in the patients who had persistent neurologic signs or symptoms. Scans were positive as early as Day 3. No patient's initial scan after that time was normal. The time of maximum uptake ranged from approximately 1½ to 6 weeks. The scans remained positive longer in this group than in those who recovered completely, 1 remaining positive as long as Day 77. Taking an arbitrary 2-week point, with only 3 exceptions, scans became more dense shortly after this period. Six patients were not included in the above time-density relationship because the onset of illness was not clearly defined.

TABLE II

LOCATION OF UPTAKE

	Left	Right
Crescent only	1	0
Frontal	5	3
Fronto-parietal	4	0
Parietal	2	1
Occipital	2	0
Sylvian fissure	7	4
Posterior fossa	1	1
Total 31	22	9

TIME-DENSITY CLINICAL CORRELATION

Figure 3 shows the correlation of prognosis to the change in scan density and change in the patient's clinical condition. There were 5 patients who improved clin-

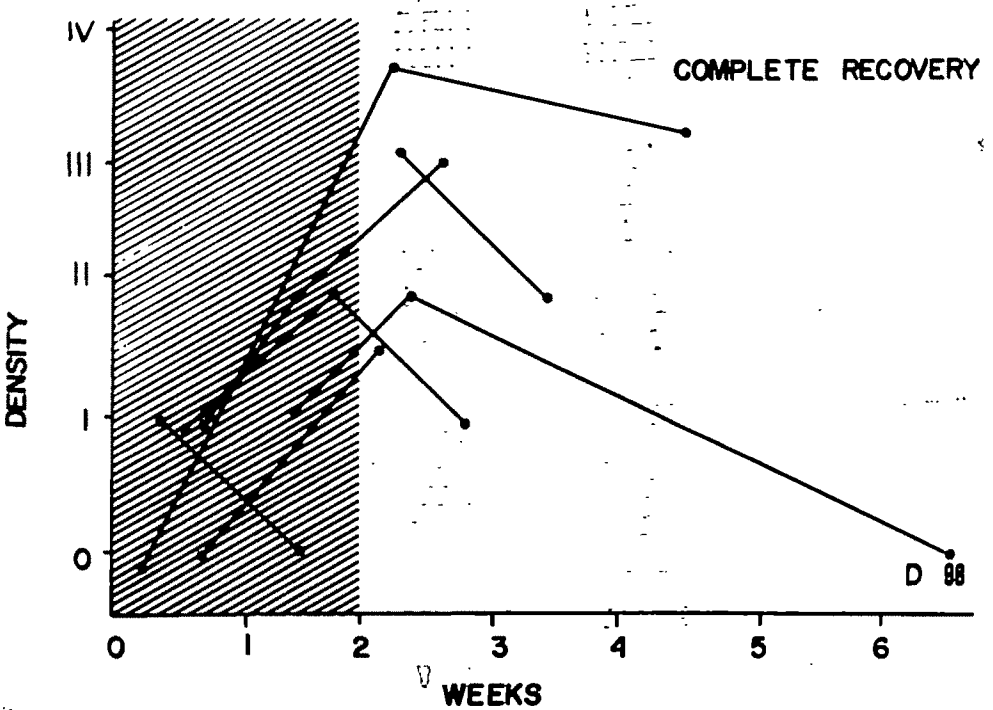


FIG. 1. Time-density relationship in 7 patients who recovered completely. Each dot represents a separate scan. The scans tend to become less dense after 2 weeks.

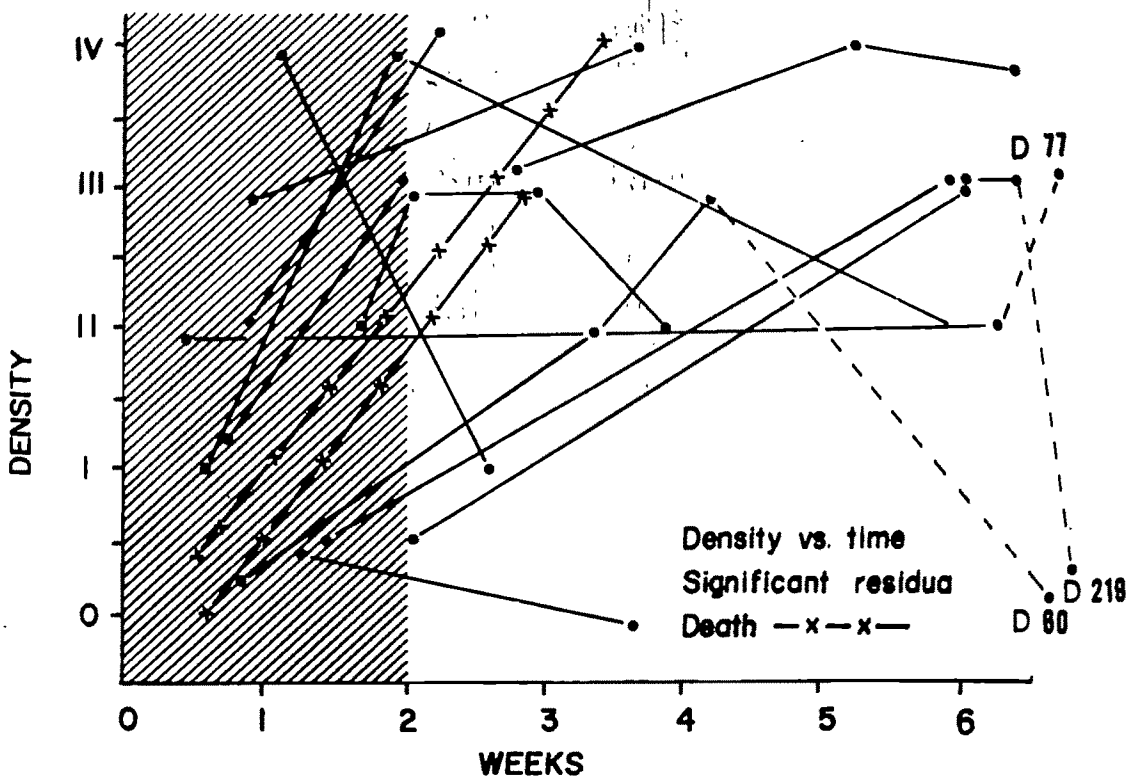


FIG. 2. Time-density relationship in 15 patients who had persistent neurologic signs or symptoms. The scans remained positive longer in this group and tended to become denser after 2 weeks.

ically, while the scan density diminished; they were all discharged asymptomatic. However, when the patient improved clinically, but the scan became more dense, only 4 of 13 were discharged asymptomatic. Every patient who deteriorated clinically in the period between these 2 scans was discharged with residual symptoms or died. Patients whose clinical course or scan remained stable did not recover in the duration of the study.

Density Alone. The maximum scan density *versus* outcome is illustrated in Figure 4. Four of 7 patients with a maximum scan density rating of II recovered completely, while only 3 of 12 patients with a maximum scan density rating of III and 1 of 7 with a density scan rating of IV recovered completely. Generally, the more dense the scan, the worse the prognosis. However, there were complete recoveries, significant residua, and deaths in each group except those with a density rating of I.

Area Alone. Figure 5 shows the clinical severity at onset as plotted against the area of abnormal uptake. No significant relationship was found.

Figure 6 shows the relationship between area and prognosis. There is a trend toward a poorer prognosis with larger areas of abnormal uptake.

DISCUSSION

The mechanism of increased isotope uptake by cerebral infarction is even less well understood than that by intracranial neoplasm.[1,7,8]

Increased vascularity occurs in cerebral infarction, especially during the healing process. Immediately after the obstruction, blood flow ceases. Anastomotic vessels open up due to local accumulation of metabolic products and pressure in adjacent arteries. Later the infarction is characterized by softening, necrosis and healing by astroglial response and apparent proliferation of cap-

	NO RESIDUA	RESIDUA	DIED
PATIENT IMPROVED SCAN LESS DENSE	5	0	0
PATIENT IMPROVED SCAN DENSER	4	8	1
PATIENT WORSE SCAN LESS DENSE	0	2	1
PATIENT WORSE SCAN DENSER	0	1	1
PATIENT SAME SCAN LESS DENSE	0	2	0
PATIENT IMPROVED SCAN SAME	0	3	0

FIG. 3. Correlation between change in scan density, clinical course and prognosis. All patients who improved clinically while the scan became less dense were discharged symptom-free.

illaries.[2] These capillaries are abnormal and permeable to normal plasma constituents, pertechnetate and other radiopharmaceuticals.

It has been postulated that edema plays a different role in cerebral infarction than in tumor. It is present within a few hours, earlier than the scan becomes positive. It is possible that the edema compresses the vessels leading into and through the lesion and prevents the isotope from reaching the abnormal area in the early stages. Later, in a week or two when the edema subsides, the isotope is no longer excluded. This may explain the absence of early radioisotope uptake.

We suggest the following sequence of events: Initially the vessel is occluded. Later the thrombus or embolus is either resorbed or propagated distally, subjecting

	NO RESIDUA	RESIDUA	DIED
I	2	0	0
II	4	2	1
III	3	8	1
IV	1	5	1

FIG. 4. Maximum scan density *versus* prognosis. In general, the denser the maximum scan abnormality, the worse the prognosis.

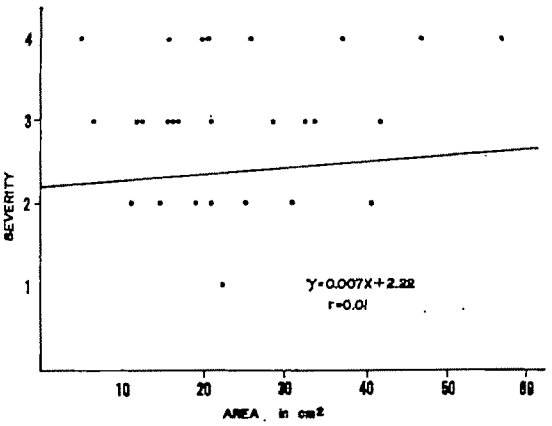


Fig. 5. The clinical state at onset by the criteria of Table 1 is related to the area of uptake. There is poor correlation between the two.

the lesion to arterial pressure.[3] At first the edema prevents the inflow of isotope into the region of increased capillary permeability. One to two weeks later, the edema is subsiding, the capillaries are proliferating, and the isotope uptake has become maximal. Months later the healing process has ceased and the scan has returned to normal.

There are certain characteristics of the isotopic examination which may be helpful in differentiating infarction from tumor—a difficult problem, especially in the elderly patient. These are the location and the time variation of the isotope uptake.

In our experience, the abnormality of infarction has always reached the convexity of the brain as seen in the frontal or posterior projections. This is probably because of the greater vascularity of the gray matter compared to the white matter.[2] In those cases where it was separable from the periphery, the lesion was neoplastic. However, the pattern of uptake itself is not diagnostic. There are areas which may be poorly or well defined or of any intensity, reflecting the uneven distribution of the isotope through the lesion.

The second point of differentiation is that tumors rarely exhibit rapid changes in scan density. If change occurs it is in the direction of greater density. Tumor hemorrhage may add to tumor uptake of radiopharmaceuticals, presumably by the same mechanism as infarction. This may resolve, with the scan becoming less positive with time. We have only observed 1 such case.

Consequently, in cases of uncertain diagnosis, our procedure is to perform a scanning as soon as a patient is admitted to the hospital and repeat it 7 to 10 days later. The incidence of positive scans in the first week has been reported to be 27 per cent, with an over-all positive incidence of 75 per cent.[5] Most brain tumors would exhibit a positive scan on the day of admission and change little in the next week.

A changing isotope pattern after the second week has been shown to be a useful indication of prognosis. For this reason, we recommend a third study approximately 3 to 4 weeks after the onset of symptoms. Increasing scan density shortly after 2 weeks indicates prolonged morbidity.

The serial scan density change is more meaningful if the clinical course is taken into account between the 2 scannings. All patients who improved clinically while the scan became less dense were discharged without residua.

In general, the more dense the scan the worse the prognosis. In itself, however, this is not a reliable sign. A large area of abnormal uptake tended to imply a poor prognosis, but bore almost no relationship to the severity of the disease at the onset.

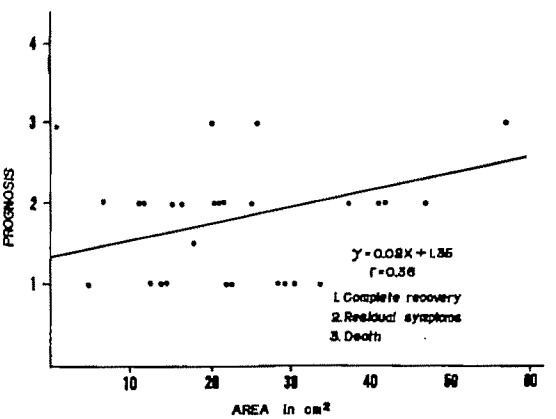


Fig. 6. Trend of poor prognosis with large areas of abnormal uptake.

SUMMARY

The serial scans and case histories of 28 patients with cerebral infarction were reviewed.

The correlation of changing scan patterns with clinical course was a useful guide to prognosis. Scan area and density alone were of limited value.

It is recommended that a scanning be performed as soon as possible after the onset of symptoms as a baseline, 7 to 10 days later for diagnosis, and at 3 to 4 weeks for prognosis.

Michael S. Usher, M.D.
Department of Radiology
Wesley Memorial Hospital
250 East Superior Street
Chicago, Illinois 60611

REFERENCES

1. BAKEY, L. Basic aspects of brain tumor localization by radioactive substances: review of current concepts. *J. Neurosurg.*, 1967, *27*, 239–245.
2. BLACKWOOD, W., MCMENEMAY, W. H., MEYER, A., NORMAN, R. M., and RUSSELL, D. S. Greenfield's Neuropathology. Second edition. Williams & Wilkins Company, Baltimore, 1966.
3. FISHER, M., and ADAMS, R. D. Observations in brain embolism with special reference to mechanism of hemorrhagic infarction. *J. Neuropath. & Exper. Neurol.*, 1951, *10*, 92–94.
4. HARPER, P. V., BECK, R., CHARLESTON, D., and LATHROP, K. S. Optimization of scanning method using technetium-99m. *Nucleonics*, 1964, *22*, 50–54.
5. MOLINARI, G. F., PIRCHER, F., and HEYMAN, A. Serial brain scanning using technetium^{99m} in patients with cerebral infarction. *Neurology*, 1967, *17*, 627–636.
6. OVERTON, M. C., III, HAYNIE, T. P., and SNODGRASS, S. R. Brain scans in nonneoplastic intracranial lesions: scanning with chlormerodrin Hg 203 and chlormerodrin Hg 197. *J.A.M.A.*, 1965, *191*, 431–436.
7. QUINN, J. L., III. Brain Scanning in Cerebral Vascular Disease. Sixth Princeton Conference on Cerebral Vascular Disease. Grune and Stratton, Inc., New York, 1968, pp. 179–194.
8. TATOR, C. H., MORLEY, T. P., and OLSZEWSKI, J. Study of factors responsible for accumulation of radioactive iodinated human serum albumin (RIHSA) by intracranial tumours and other lesions. *J. Neurosurg.*, 1965, *22*, 60–76.
9. WILLIAMS, J. L., and BEILER, D. Brain scanning in non-tumorous conditions. *Neurology*, 1966, *16*, 1159–1166.

RADIATION RESPONSE IN RELATION TO THE CELL CYCLE *IN VIVO**

By JACOB I. FABRIKANT
BALTIMORE, MARYLAND

THE response of a proliferating cell population to ionizing radiation depends, to a large degree, on the distribution of the cells as a function of their position in the cell cycle.[14,45,46] Proliferating cell systems are normally compartmentalized, and the cell cycle may be divided into 4 phases: the presynthetic period, G_1; the DNA synthetic period, S; the postsynthetic period, G_2; and the period of mitosis, M.[27,30] In most mammalian cell systems examined, the duration of the cell cycle and of its phases are somewhat invariant; the duration of S is ~6 to 10 hours, G_2~1 to 2 hours, M ~1 hour, but the duration of G_1 may vary greatly among the different tissues and is primarily responsible for the variation in cell cycle times among different proliferating cell systems.[38,42,43]

The radiation responses in mammalian cells, such as modification to DNA synthesis, mitotic and division delay, and the production of chromosome aberrations affecting the proliferative capacity, depend, in part, on the cell cycle phase at the time of irradiation.[14,45,46] Most of the studies in the past were made primarily by irradiating synchronized populations of cells *in vitro* and differences in responses of different cell lines, in the synchrony methods, in dose levels, and in parameters measured, have made interpretations of these elegant experiments difficult.

In order to examine the radiation response within the mammalian cell cycle *in vivo*, however, it would be of value to synchronize the cell population so that cells are of the same age in their progression through the cell cycle. The liver is a conditional cell renewal system which ordinarily undergoes little renewal, but may do so in response to a demand situation to compensate for loss of cells—for example, after partial hepatectomy. Previous studies in this laboratory[16,19–22] have shown that in young rats, partial hepatectomy resulted in a large near-synchronous cohort of cells progressing through a period of increased RNA synthesis beginning within 6 hours, followed by an onset of increased DNA synthesis at 15 to 16 hours, and lasting approximately 9 to 11 hours, and by a wave of mitoses beginning at about 26 to 28 hours. Peaks of synthetic activity occurred between 24 and 26 hours, and of mitotic activity, between 32 and 34 hours. Allowing for an immediate postoperative lag phase due to shock and anesthesia lasting only a few hours or less, the progress of the liver cells was from a relative resting (G_0) phase, through a G_1 period of somewhat less than 10 hours, an S period ~8 hours, a G_2 period of ~2 to 3 hours, and an M period of ~1 hour (Fig. 1). The duration of the G_1-S-G_2-M sequence was ~20 to 24 hours, the spread being due apparently to variation within the G_0 and G_1 compartments.[22]

The regenerating liver provides an attractive *in vivo* system to study the influence of cell cycle stage on radiation response. Previous studies on radiation-induced changes of biochemical and physiologic events leading to parenchymal cell proliferation in the regenerating liver demonstrated that depending on the radiation dose and the time of exposure, radiation delayed the onset of DNA synthesis

* Presented, in less detailed form, at the Sixteenth Annual Meeting of the Association of University Radiologists, Columbus, Ohio, May 8–11, 1968.

From the Departments of Radiological Science and Radiology, The Johns Hopkins University, Baltimore, Maryland.

Research was supported, in part, by grants GM 10802-06 and 5 TO1 GM 01328-03 from the National Institutes of Health, United States Public Health Service, and AT (30-1) 3970 from the United States Atomic Energy Commission.

and cell division primarily by impairing the production of DNA precursors; once DNA synthesis began, much larger doses were required to suppress cell proliferation.[11–22] In the following studies to be reported, tritiated thymidine (TdR-H^3) pulse-labeling techniques, mitotic counts and chromosome squashes have been used to examine the variation of radiation sensitivity within the parenchymal cell cycle *in vivo* by examining the patterns of modification to DNA synthesis, mitotic and division delay* and the production of chromosomal aberrations affecting the proliferative capacity of the tissue.

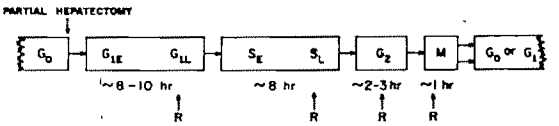


FIG. 1. Scheme of the first parenchymal cell cycle after synchronization (partial hepatectomy) in the McCollum rat. The cell cycle contains 4 phases (G_1, presynthetic phase; S, DNA synthesis phase; G_2, postsynthetic phase; M, mitosis).[42] The G_1 and S phases may be further structured into early and late; *viz.*, G_{1E} and G_{1L}, and S_E and S_L, respectively. The G_0 cells of the resting liver comprise the potentially proliferative population which may be synchronized into cell cycle by partial hepatectomy.[19–22] The approximate durations of the phases of the cell cycle are shown, and based on the data, the times of irradiation (R) during the different phases of the cell cycle are indicated.

MATERIALS AND METHODS

Animals. The animals used were 6 to 8 week old inbred McCollum strain male rats weighing 90 to 110 gm., bred in The Johns Hopkins University School of Hygiene and Public Health. Control and irradiated rats were housed in groups of 4 in stainless steel cages and fed food (Purina laboratory chow) and water *ad libitum.*

Partial hepatectomy. Partial hepatectomy consisted of the surgical removal of the median and left lateral lobes of the liver;[24] there was no surgical mortality. Since little or no diurnal variation occurs in percentage labeling and mitotic indices in the resting liver,[16,22] the times of irradiation were 10:00 A.M. or 3:00 P.M. and the time of partial hepatectomy varied to obtain the proper interval between synchronization and irradiation. From liver weight measurements on control animals, ~65 per cent of the liver was removed by the hepatectomy technique.

Irradiation technique. Animals were irradiated in groups of 8 in lucite chambers,[15] using a 2 mev. van de Graaff unit operated at 1.8 mev. and 200 μa., half-value layer of 6.5 mm. Pb, focus-skin distance of 132 cm., at a dose-rate of 22 r/min. The total body dose was 700 rads.

Tritiated thymidine. TdR-H^3, specific activity 14.6 c/mmole,* in 100 μc/ml. solution of 0.9 per cent NaCl, was injected intraperitoneally, 50 μc per animal (~0.5 μc/gm. body weight) 1 hour prior to sacrifice. The dose of TdR-H^3 produced good autoradiographs within a 3 week exposure time, and there was no evidence of detectable radiation injury.[17,19,20,22,23,39–41]

Quantitative histology. Animals were killed in pairs or groups of 4, depending on the experiment, by heavy ether anesthesia and cervical dislocation. Since proliferating cell populations in the regenerating liver are distributed uniformly throughout the lobes of the liver remnant,[16,22] the right lobe of the liver was considered representative and used for all histologic studies. One to 2 gm. of tissue was placed in fixative (20 parts 70 per cent ethanol, 2 parts 10 per cent formalin [$CaCO_3$ in excess] and 1 part glacial acetic acid) for 24 hours, and transferred to 70 per cent ethanol. Histologic sections (4 μ) obtained from wax-embedded tissue were prepared for autoradiography on chemically clean gelatin-alum-coated microscopic slides, dipped in Ilford K-5 Nuclear† liquid emulsion (50

* Since the presence of mitotic cells and the process of cell division (cytokinesis) are both suppressed by irradiation, these effects are referred to as mitotic delay and division delay, respectively, and the durations of suppression, the delay periods. In the regenerating liver cell system *in vivo*, these two effects could not be measured independently and, therefore, mitotic delay and division delay were considered together as one response; *i.e.*, the delay in onset of cell division during the first cell cycle, and the decrease in the rate and number of cells dividing.

* New England Nuclear Corp., Boston, Massachusetts.
† Ilford Ltd., Ilford, Essex, England.

per cent emulsion and 50 per cent distilled water at 45°C.), dried, stored with desiccant in light-tight boxes, and exposed for 3 weeks at 4°C. Slides were developed in Kodak D19 developer and fixed,* then washed, stained with hematoxylin and eosin and mounted. In slides with background counts of less than 1 to 2 grains per nucleus, parenchymal cell nuclei with more than 10 grains were scored as labeled. Percentage labeling and mitotic indices were determined in counts of 5,000 to 7,500 cells in each liver.

Chromosome preparations. About 1 gm. of tissue was finely minced with scissors, placed in cold (4°C.) chromosome fixative (6 parts methanol, 3 parts chloroform, 2 parts proprionic acid) and stored in fresh fixative at 4°C. for 24 hours.[8,9] Squash preparations were made to about a single cell layer using a standard dry ice technique, stained with 2 per cent acetic-orcein, dried, and mounted.[17,20]

RESULTS

Unirradiated rats. The pattern of 1 hour percentage labeling and mitotic indices of parenchymal cells at frequent intervals during the 40 hours after synchronization is shown in Figure 2. Labeled cells were first seen after 12 hours; there was a rapid rise to ~40 per cent by 24 to 28 hours, and a gradual fall to ~15 per cent by 40 hours. Cell division began after 20 hours; the mitotic index rose to ~4.0 per cent by 32 to 36 hours, then declined to ~2.0 per cent by 40 hours. Waves of cells in division followed those in DNA synthesis by ~8 hours; allowing for this interval, there were some ten times as many cells labeled as in mitosis (areas under the curves). These data on the McCollum rat, and those of previous studies on the August rat,[21,22] indicate that following synchronization by partial hepatectomy, parenchymal cells were "triggered" from a resting or dormant G_0 phase, through a G_1-S-G_2-M generation cycle phase sequence lasting ~20 to 24 hours. Following a postoperative lag, the duration of G_1 was ~10 hours; S, ~8 hours; G_2, ~2 to 3 hours; and M, ~1 hour.[22]

Irradiated rats. Based on these durations, the age-response pattern was determined during the different phases of the cell cycle. Late G_1 cells (G_{1L}) were irradiated at 14 hours; late S cells (S_L) at 25 hours; G_2 cells at 30 hours; M cells at 32.5 hours; and G_0 cells were irradiated prior to partial hepatectomy (Fig. 1).

Irradiation at 14 hours (mainly G_{1L} cells) delayed the onset of DNA synthesis and cell division by ~8 to 12 hours, and decreased the number of cells proliferating and the rate of cells entering synthesis and mitosis (Fig. 3). Cells may have been retained longer in the S period, possibly due to a decreased rate of DNA synthesis per cell. There was no evidence of stimulation of G_{1L} cells into S. After the mitotic

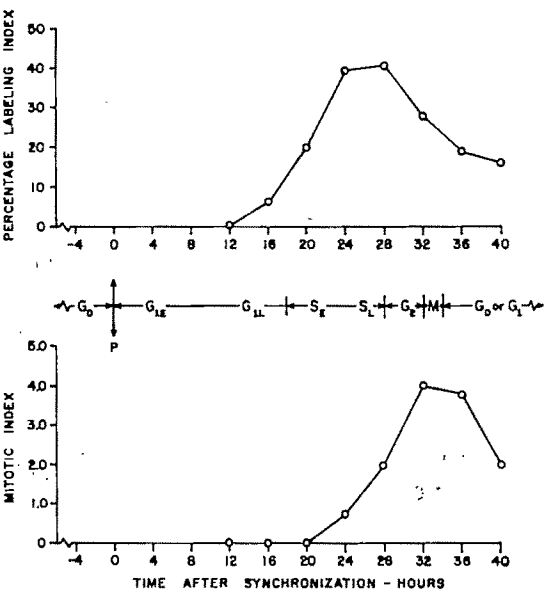


FIG. 2. *Upper.* The temporal pattern of 1 hour TdR-H^3 labeling indices in proliferating liver parenchymal cells at frequent intervals during the 40 hours after synchronization. *Lower.* The temporal pattern of parenchymal cell mitoses in the liver at frequent intervals during the 40 hours after synchronization. The mean values for 2 rats at each interval are shown. Based on these data, the durations of the phases of the cell cycle, G_1, S, G_2, M, were determined.[22]

* Eastman Kodak Co., Rochester, New York.

delay, the mitotic index continued to rise once cell division began.

Irradiation at 25 hours (mainly S_L cells with a few G_2 cells) decreased the fraction of cells synthesizing DNA initially, and may have decreased the rate of synthesis per cell (Fig. 4). The total amount of DNA synthesized by 40 hours (areas under the curves) was only slightly affected. However, cell division was markedly depressed, and mitotic and division delay were manifested both as a decrease in rate and number of cells dividing by 40 hours.

Irradiation at 30 hours (mainly G_2 cells with a few S_L and M cells) caused the most marked mitotic and division delay, and a decreased rate and number of cells dividing (Fig. 5). The initial depression of the percentage labeling index by about one-third at 32 hours was primarily an effect on the S_L cells.

Irradiation at 32.5 hours (a mixture of M cells and some S_L and G_2 cells) provided the least precise information (Fig. 6).

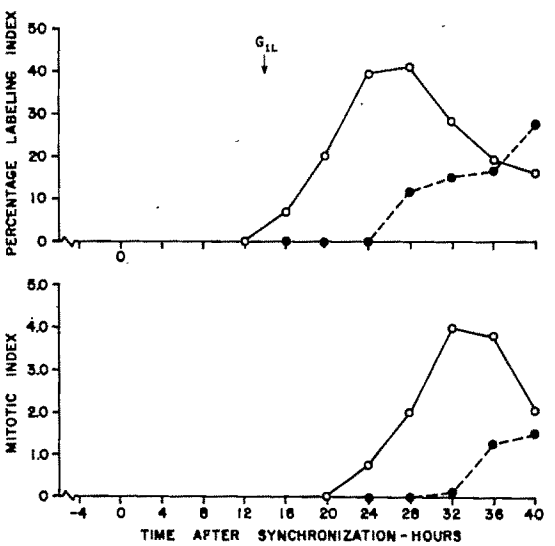


Fig. 3. Modification to DNA synthesis and mitotic and division delay in proliferating parenchymal cells irradiated (700 rads) 14 hours after synchronization (mainly G_{1L} cells). *Upper.* TdR-H^3 labeling indices after synchronization and irradiation. *Lower.* Mitotic indices after synchronization and irradiation. The mean values for 2 rats at each interval are shown for unirradiated (open circles) and irradiated (closed circles) animals.

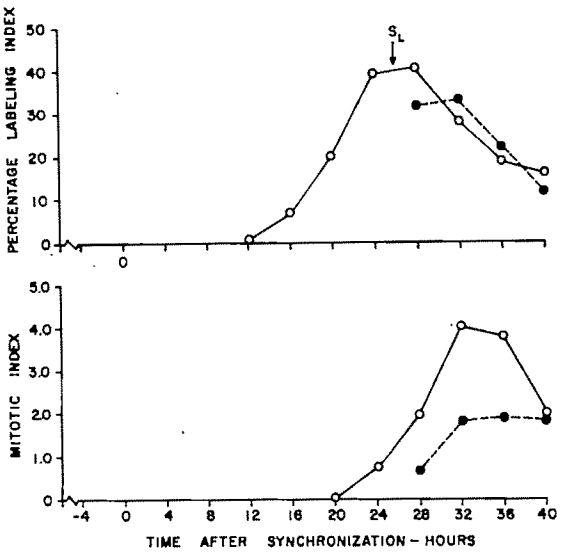


Fig. 4. Modification to DNA synthesis and mitotic and division delay in proliferating parenchymal cells irradiated (700 rads) 25 hours after synchronization (mainly S_L cells). *Upper.* TdR-H^3 labeling indices after synchronization and irradiation. *Lower.* Mitotic indices after synchronization and irradiation. The mean values for 2 rats at each interval are shown for unirradiated (open circles) and irradiated (closed circles) animals.

There may have been a slight depression of DNA synthesis in the S_L cells present, but the data are not sufficient. However, there was marked mitotic and division delay, the number of cells in division being reduced by ~50 per cent by 3.5 hours after irradiation.

Additional information on the response of the dormant G_0 cell population was obtained from previous studies on the effect of continuous irradiation at approximately 50 rads/day for 14 days (total dose, 700 rads) on regenerating liver cell proliferation in the young August strain male rat[19] (Fig. 7). There was a delay of ~4 hours in the onset of DNA synthesis and of cell division, there was some decrease in the rate and number of cells proliferating, but little effect on the rate and number of cells entering mitosis.

Chromosome aberrations. Anaphase-telophase squash preparations did not provide the detail necessary for identifying with certainty all chromosome or chromatid

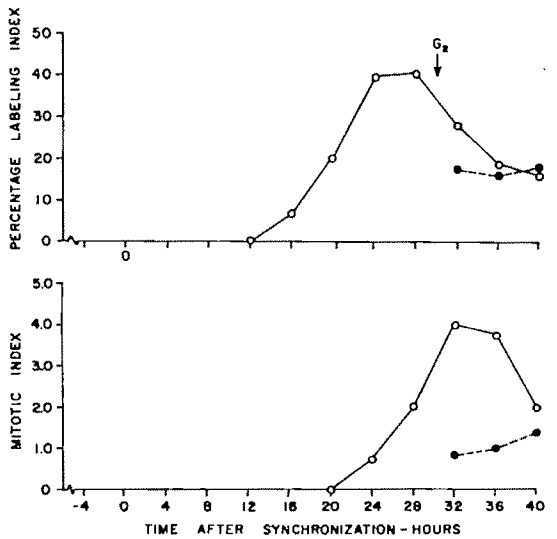


FIG. 5. Modification to DNA synthesis and mitotic and division delay in proliferating parenchymal cells irradiated (700 rads) 30 hours after synchronization (mainly G_2 cells, with some S_L and early prophase cells). *Upper.* TdR-H^3 labeling indices after synchronization and irradiation. *Lower.* Mitotic indices after synchronization and irradiation. The mean values for 2 rats at each sacrifice interval are shown for unirradiated (open circles) and irradiated (closed circles) animals.

aberrations produced. Thus, aberrations were considered as chromosomal (Fig. 8*A*), and no attempt was made to classify according to type. Figure 9 illustrates the age-response of chromosomal aberrations produced during the first division cycle. The frequency was greatest when cells were irradiated in G_2 (62 per cent) followed in order by cells irradiated in G_{1L} (45 per cent), in S_L (22 per cent), and in M. For M cells, precise data are not available. Additional information on G_0 liver cells in rats continuously irradiated at 50 rads/day for 14 days (*i.e.*, only a small fraction of the duration of the cell cycle in the resting liver) indicated that the frequency of chromosomal aberrations was less than 25 per cent, or about the same as relatively resistant S_L cells.[21]

Degenerated and fragmented cells undergoing early necrobiosis prior to division were readily identified in chromosomal preparations, but only when cells were irradiated in G_2 (Fig. 8*B*).

DISCUSSION

Figure 9 summarizes the age-response to irradiation in proliferating parenchymal cells *in vivo* with regard to modification to cell proliferation—DNA synthesis and mitotic and division delay—and chromosomal aberrations. The former responses were greatest in late G_1 cells, less in G_2 cells, and least in late S and G_0 cells. Chromosomal injury was greatest when cells were irradiated in G_2, less in late G_1, and least in late S and G_0. The sensitivity of G_2 cells was further marked by early necrobiosis during interphase. It was difficult to assess the responses occurring in M cells, since the data are not precise.

The pattern of cell proliferation after partial hepatectomy provided a relatively high degree of cell synchronization in DNA synthesis and cell division.[21,22] There is evidence available that during regeneration, proliferative activity was preceded

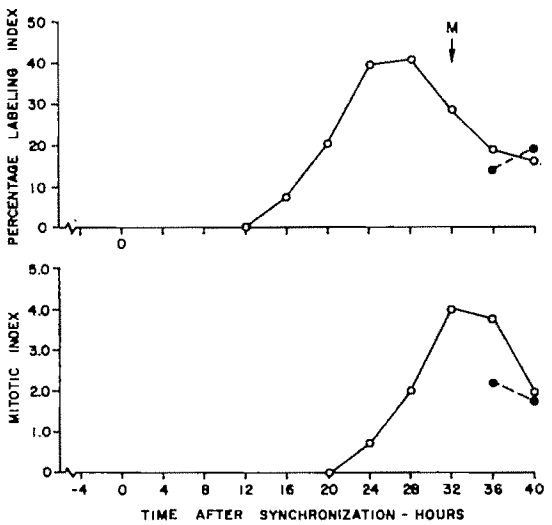


FIG. 6. Modification to DNA synthesis and mitotic and division delay in proliferating parenchymal cells irradiated (700 rads) 32.5 hours after synchronization (a mixture of mainly M and G_2 cells, with some S_L cells of the first cell cycle, and a few early G_1 cells of the second cell cycle). *Upper.* TdR-H^3 labeling indices after synchronization and irradiation. *Lower.* Mitotic indices after synchronization and irradiation. The mean values for 2 rats at each interval are shown for unirradiated (open circles) and irradiated (closed circles) animals.

by metabolic changes; DNA synthesis began ~8 hours prior to cell division, and enzymes required for the production of DNA precursors—protein and RNA—could be demonstrated a few hours prior to the onset of DNA synthesis (for review[6]). Radiation effects on cell proliferation in the regenerating liver following single and repeated doses have been studied in the past using techniques of chemical assay, the incorporation of labeled protein, RNA and DNA precursors, and changes in mitotic indices.[3,6,33,52,53] It has been demonstrated that the synthesis of enzymes, such as thymidine kinase, required for the production of DNA precursors, was delayed or impaired when irradiation was given several hours before the onset of DNA synthesis, *i.e.*, during the G_1 period. Doses of 500 rads to 1,000 rads given before or during the early stages of regeneration—during the G_0 phase and the early G_1 phase, respectively—caused a lag

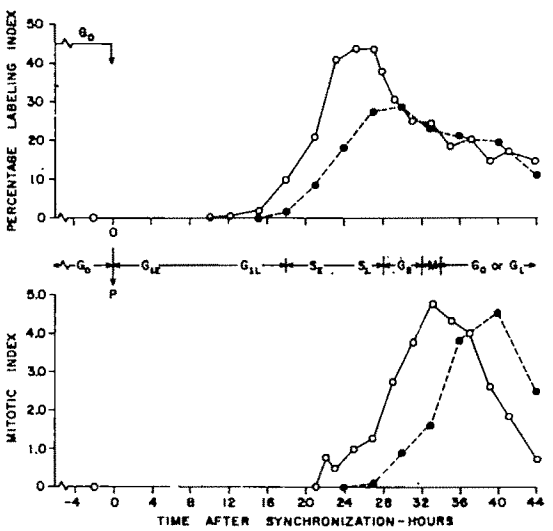


FIG. 7. Modification to DNA synthesis and mitotic and division delay in proliferating parenchymal cells in August rats continuously irradiated at 47 rads/day for 15 days (700 rads) prior to synchronization (mainly G_0 cells) 2 hours after the completion of the exposure period. *Upper.* TdR-H^3 labeling indices after irradiation and synchronization. *Lower.* Mitotic indices after irradiation and synchronization. The mean values for 4 rats at each interval are shown for unirradiated (open circles) and irradiated (closed circles) animals..

in the initiation of enzyme (*e.g.*, thymidine kinase and DNA polymerase) and DNA synthesis and cell division. Doses of 150 rads to 450 rads given during the first 10 to 12 hours of regeneration caused some delay in the synthesis of proteins and DNA.[1–7,25,26,28,33,37] Once DNA synthesis began (*i.e.*, early S cells) much larger doses were required to depress cell proliferation.[14,25,26,28,33,52]

Bollum and his colleagues[4,5] have shown that the level of thymidine kinase, rather than DNA polymerase, limited the rate of DNA synthesis; irradiation at 6 hours after hepatectomy, but before thymidine kinase formation or DNA synthesis occurred (the G_{1E} period), markedly reduced the level of kinase and polymerase at 30 hours of regeneration. Irradiation at 16 hours (the G_{1L} period), after kinase and polymerase were produced, had little effect on subsequent enzyme levels. DNA synthesis was relatively resistant to radiation once synthesis began. In the synchronized liver cell system *in vivo*, therefore, it appeared that (1) irradiation early in the G_1 period markedly inhibited enzyme systems responsible for DNA synthesis; (2) irradiation in the G_{1L} period or in the S_E period had relatively little effect on DNA synthesis, since the necessary enzymes were formed and were relatively insensitive to radiation injury; (3) irradiation in S_L had least effect on subsequent cell proliferation.

The most commonly observed radiation response on proliferating mammalian cell systems *in vivo* is mitotic delay; cells irradiated after DNA synthesis but before mitosis are prevented from the orderly progression from the G_2 period through mitosis.[14,38] This mitotic inhibition indicates that cells are blocked somewhere between the termination of DNA synthesis and late prophase. The duration of the G_2 block is dependent on the type of cell system, on the radiation dose, and on the length of the cell cycle.[38] In general, cell division is more sensitive than DNA synthesis, so that mitotic inhibition is more prolonged than suppression of DNA syn-

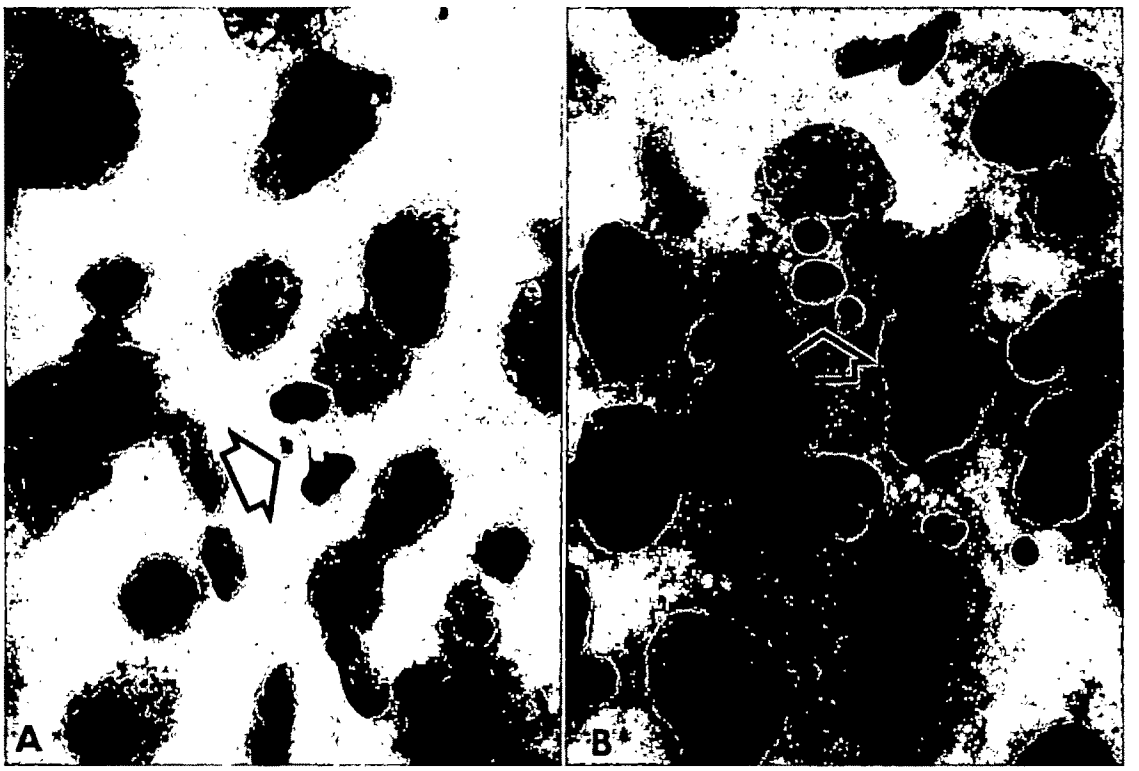


FIG. 8. Chromosomal and cytologic damage in proliferating parenchymal cells irradiated (700 rads) 30 hours after synchronization (mainly G_2 cells) and examined at 33 hours. (*A*) Anaphase-telophase cell with chromosomal bridge and excluded chromatid fragments (1,800 ×; acetic-orcein). (*B*) Early necrobiosis—clumped, spherical chromatin fragments dispersed in liver tissue (1,800 ×; acetic-orcein).

thesis. A G_1 block, on the other hand, will suppress the initiation of DNA synthesis, *i.e.*, the transition of cells from the G_1 phase to the S phase; the response will also be manifested as a blocked mitosis, but the mitotic delay period will usually be hours longer than the G_2 block. The G_2 block, therefore, is independent of DNA synthesis, whereas mitotic and division delay may occur also as a result of cells irradiated in G_1 and S.[14,46,47]

Radiation effects on the cell cycle in vitro. Studies on age-response to radiation in proliferating cell systems *in vitro* are much more precise because of the reliable methods for synchronization, and the use of TdR-H^3 labeling techniques and mitotic indices for measurements of changes in rates and transitions as irradiated cells progress through phases of the generation cycle.[10,13,14,46,47] Sinclair[46,47] has reviewed studies on radiation responses in single cells *in vitro*, such as effects on growth, survival (colony-forming ability), incorporation of labeled precursors (modifications to DNA synthesis), mitotic and division delay, and chromosomal aberrations affecting survival. The age-responses in cultured mammalian cells, in general, were very similar, although some differences existed, depending on the cell line, the methods of synchronization, and the radiation dose.[10,44,50] Survival data indicated that for cells with short cell cycle times (*e.g.*, mouse L cells), G_2 and M cells were most sensitive, G_1 cells less sensitive, and late S cells least sensitive.[11,12,54,55] In cells with long cell cycle times (*e.g.*, HeLa and Chinese hamster cells), early G_1 cells were relatively resistant, whereas late G_1 cells

were sensitive.[45,48,49,51,59] Modification to DNA synthesis—delay in transition from the G_1 to S period, and reduction in the rate and prolongation of the S period—was little affected by irradiation in G_1 and G_2. The response was greatest when cells were irradiated in S, although there was only a slight effect in the total amount of DNA synthesized. Similar changes have been observed in human bone marrow cells cultured *in vitro*[29] and in intestinal crypt cells and seminiferous epithelium *in vivo*.[32,35,36]

Chromosome aberrations affecting survival. Radiation-induced chromosomal aberrations in mammalian cells depend on the stage of the cell cycle at the time of irradiation; G_1 and early S cells yield chromosome aberrations, while late S and G_2 cells give rise to chromatid aberrations. In general, experiments on age-responses in plant cells (*e.g.*, *Tradescantia* microspores and *Vicia faba* root tips) and mammalian cells (*e.g.*, Chinese hamster cells) *in vitro* have shown that chromosomal aberrations produced by irradiation varied in type and frequency depending on the position of the cell in the cell cycle.[10,14,31,34,44,46,56–58] Cells in G_1 were relatively less sensitive than those in early and late S, whereas G_2 cells were most sensitive. In other mammalian cell systems, S cells were slightly more sensitive than G_2 cells, but in general, G_1 cells were the least sensitive.[11,12,35,46]

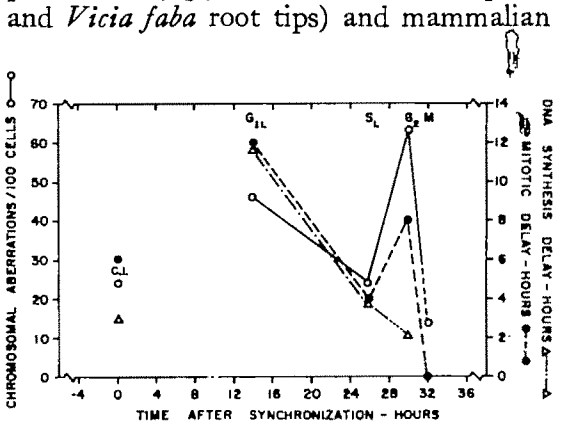


FIG. 9. Summary of age-response data. *Left ordinate and abscissa.* Radiation-induced chromosomal aberrations in anaphase-telophase cells 33 hours after synchronization; cells were irradiated at 14 hours (G_{1L} cells), 25 hours (S_L cells), 30 hours (G_2 cells) and 32.5 hours (M cells). *Right ordinate and abscissa.* Modification to DNA synthesis (DNA synthesis delay) and mitotic delay based on 1 hour TdR-H^3 labeling indices and mitotic indices at frequent intervals after synchronization and irradiation (see text). The values of the various responses of G_0 cells are included for comparison; these represent animals continuously irradiated prior to synchronization. Dotted lines are used where data are not precise and proper values cannot be determined.

The present studies *in vivo* were not as precise as *in vitro* experiments, both with regard to synchronization and to recognition of chromosomal damage at anaphase. However, the general trend of the age-response function and chromosomal aberrations in cells *in vitro* (for review[56,57]) was seen in the synchronized liver cell population; sensitivity increased from G_1, through S (there was a slight decrease in S_L cells), and was greatest in G_2. Since the age-dependence for chromosome aberrations would be directly related to lethality (or survival), it appeared that the regenerative capacity of the liver would probably be most affected when cells were irradiated in G_2. Regeneration would be further affected by lethally damaged cells which underwent early necrobiosis and disintegrated—morphologic chromatin clumping, pyknosis, and dispersion of chromatin as clusters of spherical bodies—within only a few hours after irradiation prior to cell division. Early necrobiosis has been demonstrated in several irradiated proliferating cell systems, such as intestinal epithelium, bone marrow and hair follicle,[38] and occurred in the regenerating liver only when cells were irradiated in G_2.

Finally, it must be recognized that the interval between irradiation and mitosis was different for each experiment, and the response would depend not only on the age-dependence sensitivity at the time of exposure, but on such modifying factors as oxygenation during and after irradiation, and the time available for processes of intracellular recovery and repair.

CONCLUSIONS

The radiation response of a proliferating cell system *in vivo* was related to the complex kinetics of cellular proliferation and, thus, dependent on the proliferative characteristics of the cell population. Studies on plant cells and mammalian cells in tissue culture have demonstrated that radiation effects on cells were clearly age-dependent, and the response of a cell population would depend, in part, on the cell age-distribution of the population at the time of exposure. These age-response studies are providing a better understanding of the normal events occurring in the generation cycle of proliferating cells and in cell populations. In addition, information is obtained for the interpretation of radiobiologic responses measured at the cellular level, such as effects on DNA synthesis and cell division. And finally, such experiments elucidate mechanisms of radiation effects at more complex tissue and organ levels with regard to cellular proliferation, lethality, and maintenance of cell populations and function.

In vitro studies on age-dependent radiation responses of single cells and groups of cells are extremely sophisticated, but are limited, in part, in that they require cell systems which are partially or completely synchronized with respect to DNA synthesis and cell division. However, they provide information on radiation responses —such as effects on growth and division, chromosomal injury, and biochemical damage—which are difficult to measure quantitatively *in vivo*. In practical situations *in vivo*, however, cells of all ages are normally present, distributed according to the proliferative characteristics of the population. Based on evidence from *in vitro* experiments, a study of the age-response function in mammalian tissues *in vivo* would require a large synchronized population in which cells were of the same age at any given time. Mammalian tissues are not normally conditioned to proliferate synchronously; the regenerating rat liver after partial hepatectomy, however, provides the degree of synchronization for examining the cell age-radiation response in relation to DNA synthesis and the cell cycle.

The present studies demonstrated that radiation effects on proliferating cell populations *in vivo* appeared to be age-dependent in a manner and degree similar to mammalian cells *in vitro*,[10,14,45,47] and that the response of a cell population *in vivo* to radiation would depend on the age-distribution of cells within the population at the time of exposure. Thus, in the first parenchymal cell cycle after partial hepatectomy, modification to DNA synthesis and mitotic division delay following 700 rads given at different times after synchronization were greatest in late G_1 cells, less in G_2 cells, and least in late S and G_0 cells. Radiation-induced chromosome aberrations occurred most frequently in G_2 cells, less in late G_1 cells, and least in S and G_0 cells.

As more information becomes available on age-responses to irradiation—changes in biochemical processes in the cell, division delay, chromosome injury, and cell death—a better understanding of the radiation effects on complex proliferating cell populations *in vivo* will inevitably result. It must be recognized, however, that the *in vivo* environment of the cell is very different from the *in vitro* milieu.[45,47] The response to radiation *in vivo* may be influenced by many complex factors, such as intercellular reactions in tissues, oxygen availability during and after irradiation, the efficiency of intercellular repair processes (as well as intracellular recovery), abscopal effects, and regenerative capacities of the cell populations. Clearly, much more work needs to be done on the age-dependence of radiation responses, both *in vitro* and *in vivo*, for a better understanding of the fundamental biologic and biophysical processes in cells and tissues, and of the radiation effects on the kinetics of complex cell populations.

SUMMARY

TdR-H^3 percentage labeling indices, mitotic indices, and the frequency of anaphase-telophase chromosomal aberrations have been used to examine the influence of the cell cycle stage on the response to X radiation *in vivo*. A high degree of synchronization was obtained in proliferating parenchymal cells after partial hepatectomy in the regenerating liver of the young male rat, and animals were irradiated (700 rads) prior to synchronization (G_0 cells), and at 14 hours (late G_1 cells), 25 hours (late S cells), 30 hours (G_2 cells), and 32.5 hours (M cells) after synchronization. Modification to DNA synthesis and mitotic and division delay were measured at frequent intervals during the first cell cycle after irradiation, and the frequency of chromosomal aberrations was determined during the first postirradiation cell division at 33 hours after synchronization. The data indicated that for proliferating parenchymal cells *in vivo*, modification to DNA synthesis and mitotic delay were greatest when cells were irradiated during the late G_1 phase, less in the G_2 phase, and least in the late S and G_0 phases. Radiation-induced chromosomal aberrations occurred most frequently in G_2 cells, less in late G_1 cells, and least in late S and G_0 cells. The results are discussed in terms of experimental studies on radiation effects and radiosensitivity during the generation cycle in plant cells and mammalian cells *in vitro*, and of age-response functions in relation to growth and cell division, biochemical effects of DNA synthesis, and chromosomal aberrations affecting the regenerative capacity of the proliferating parenchymal cell system.

Department of Radiological Science
The Johns Hopkins University School of Hygiene and Public Health
615 North Wolfe Street
Baltimore, Maryland 21205

I am indebted to Doctor Russell H. Morgan, Professor and Chairman of the Departments of Radiological Science and Radiology for his constant support and encouragement. I wish to thank Mrs. Carole L. Taylor, Mrs. Dorothy S. Kovar, and Mrs. Marcia L. Shane for their technical assistance, and Miss Barbara Grossman, Mr. Henri C. Hessels and Mr. Willie N. Ragsdale for help with the illustrations.

REFERENCES

1. ALBERT, M. D., and BUCHER, N. L. R. Latent injury and repair in rat liver induced to regenerate at intervals after x-radiation. *Cancer Res.*, 1960, *20*, 1514–1522.
2. BELTZ, R. E., and APPLEGATE, R. L. X-ray inhibition of enzyme changes associated with DNA synthesis of liver regeneration. *Biochem., Biophys. Res. Comm.*, 1959, *1*, 298–301.
3. BELTZ, R. E., VAN LANCKER, J., and POTTER, V. R. Nucleic acid metabolism in regenerating liver. IV. Effect of x-radiation of whole body on nucleic acid synthesis *in vivo*. *Cancer Res.*, 1957, *17*, 688–697.
4. BOLLUM, F. J., and POTTER, V. R. Nucleic acid metabolism in regenerating rat liver. VI. Soluble enzymes which convert thymidine to thymidine phosphates and DNA. *Cancer Res.*, 1959, *19*, 561–565.
5. BOLLUM, F. J., ANDEREGG, J. W., and POTTER, V. R. Nucleic acid metabolism in regenerating rat liver. VII. Effect of x-radiation on enzymes of DNA synthesis. *Cancer Res.*, 1960, *20*, 138–143.
6. BUCHER, N. L. Regeneration of mammalian liver. *Internat. Rev. Cytol.*, 1963, *15*, 245–300.
7. CATER, D. B., HOLMES, B. E., and MEE, L. K. Cell division and nucleic acid synthesis in regenerating liver of rat. *Acta radiol.*, 1956, *46*, 655–667.
8. CROWLEY, C. Personal communication.
9. CURTIS, H. J., and CROWLEY, C. Chromosome aberrations in liver cells in relation to somatic mutation theory of aging. *Radiation Res.*, 1963, *19*, 337–344.
10. DAVIES, D. R., and EVANS, H. J. Role of genetic damage in radiation-induced cell lethality. In: Advances in Radiation Biology. Edited by L. G. Augenstein, R. Mason, and M. R. Zelle. Academic Press, Inc., New York, 1966, pp. 243–253.
11. DEWEY, W. C., and HUMPHREY, R. M. Radiosensitivity and recovery of radiation damage in relation to cell cycle. In: Cellular Radiation Biology. Williams & Wilkins Company, Baltimore, 1965, pp. 340–375.
12. DEWEY, W. C., and HUMPHREY, R. M. Relative radiosensitivity of different phases in life

cycle of L-P59 mouse fibroblasts and ascites tumor cells. *Radiation Res.*, 1966, *16*, 503–530.

13. Elkind, M. M., and Sinclair, W. K. Recovery in x-irradiated mammalian cells. In: Current Topics in Radiation Research. Edited by M. Ebert and A. Howard. North-Holland Publishing Company, Amsterdam, 1965, pp. 165–220.
14. Elkind, M. M., and Whitmore, G. F. The Radiobiology of Cultured Mammalian Cells. Gordon and Breach, New York, 1967.
15. Fabrikant, I. B. Influence of prior irradiation on host susceptibility to infection with attenuated E strain of *Rickettsia prowazekii*. Ph.D. Thesis, University of Maryland, 1966.
16. Fabrikant, J. I. Spatial distribution of parenchymal cell proliferation during regeneration of liver. *Johns Hopkins Med. J.*, 1967, *120*, 137–147.
17. Fabrikant, J. I. Accumulation of chromosome damage under continuous low dose-rate exposure. *Radiology*, 1967, *88*, 767–774.
18. Fabrikant, J. I. Cell proliferation in regenerating liver of continuously irradiated mice. *Brit. J. Radiol.*, 1967, *40*, 487–497.
19. Fabrikant, J. I. Cell proliferation in regenerating liver and effect of prior continuous irradiation. *Radiation Res.*, 1968, *32*, 804–826.
20. Fabrikant, J. I. Radiation effects on conditional cell renewal system under continuous low dose-rate exposure. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1968, *102*, 811–821.
21. Fabrikant, J. I. Rate of cell proliferation in regenerating liver. *Brit. J. Radiol.*, 1968, *41*, 71.
22. Fabrikant, J. I. Kinetics of cellular proliferation in regenerating liver. *J. Cell. Biol.*, 1968, *36*, 551–565.
23. Grisham, J. W. Inhibitory effect of tritiated thymidine on regeneration of liver in young rat. *Proc. Soc. Exper. Biol. & Med.*, 1960, *105*, 555–558.
24. Higgins, G. M., and Anderson, R. M. Experimental pathology of liver. I. Restoration of liver of white rat following partial surgical removal. *Arch. Path.*, 1931, *12*, 186–202.
25. Holmes, B. E. Influence of radiation on metabolism of regenerating rat liver. In: Ionizing Radiations and Cell Metabolism. Edited by G. E. W. Wolstenholme and C. M. O'Connor. J. & A. Churchill, Ltd., London, 1956, pp. 225–238.
26. Holmes, B. E., and Mee, L. K. Inhibition of DNA synthesis by irradiation with special references to irradiation in early stages of liver regeneration. In: Radiology Symposium. Edited by Z. M. Bacq and P. Alexander. Butterworth & Company, Ltd., London, 1955, pp. 220–224.
27. Howard, A., and Pelc, S. R. Synthesis of deoxyribonucleic acid in normal and irradiated cells and its relation to chromosome breakage. *Heredity*, 1953, Suppl. 6, pp. 261–273.
28. Kelly, L. S. Radiosensitivity of biochemical processes. In: Fundamental Aspects of Radiosensitivity. Brookhaven Symposia in Biology, No. 14, 1961, Upton, N. Y., pp. 32–52.
29. Lajtha, L. G. Culture of human bone marrow *in vitro:* reversibility between normoblastic and megaloblastic series of cells. *J. Clin. Path.*, 1952, *5*, 67–85.
30. Lajtha, L. G., Oliver, R., and Ellis, F. Incorporation of ^{32}P and adenine ^{14}C into DNA by human bone-marrow cells *in vitro*. *Brit. J. Cancer*, 1954, *8*, 367–379.
31. Leong, G. F., Pessotti, R. L., and Krebs, J. S. Liver cell proliferation in x-irradiated rats after single and repetitive partial hepatectomy. *J. Nat. Cancer Inst.*, 1961, *27*, 131–143.
32. Lesher, S. Compensatory reactions in intestinal crypt cells after 300 roentgens of cobalt-60 gamma-irradiation. *Radiation Res.*, 1967, *32*, 510–519.
33. Looney, W. B. Replication of desoxyribonucleic acid in hepatocytes. *Proc. Nat. Acad. Sc. U. S.*, 1960, *46*, 690–708.
34. Ma, T. H., and Wolff, S. Far red induced mitotic delay and apparent increase of x-ray induced chromatic aberrations in *Tradescantia* microspores. *Radiation Botany*, 1965, *5*, 293–298.
35. Monesi, V. Relation between x-ray sensitivity and stages of cell cycle in spermatogonia of mouse. *Radiation Res.*, 1962, *17*, 809–838.
36. Oakberg, E. F. Sensitivity and time of degeneration of spermatogenic cells irradiated in various stages of maturation in mouse. *Radiation Res.*, 1955, *2*, 369–391.
37. Okada, S., and Hempelmann, L. H. Enzymatic activity related to DNA synthesis in regenerating liver of irradiated rats. *Int. J. Radiation Biol.*, 1959, *1*, 305–311.
38. Patt, H. M., and Quastler, H. Radiation effects on cell renewal and related systems. *Physiol. Rev.*, 1963, *43*, 357–396.
39. Post, J., and Hoffman, J. Some effects of tritiated thymidine as a deoxyribonucleic acid label in rat liver. *Radiation Res.*, 1961, *14*, 713–720.
40. Post, J., and Hoffman, J. Dose-dependent effects of H^3TDR as a DNA label on replication of liver cells in growing rat. *Radiation Res.*, 1965, *26*, 422–441.
41. Post, J., and Hoffman, J. Late effects of H^3TDR as a DNA label on liver cell replication. *Radiation Res.*, 1967, *30*, 748–758.
42. Quastler, H. Analysis of cell population kinetics. In: Cell Proliferation. Edited by L. F. Lamerton and R. J. M. Fry. Blackwell

Scientific Publications, Oxford, 1963, pp. 18–32.
43. Quastler, H., and Sherman, F. G. Cell population kinetics in intestinal epithelium of mouse. *Exper. Cell. Res.*, 1959, *17*, 420–438.
44. Scott, D., and Evans, H. J. X-ray induced chromosomal aberrations in *Vicia faba:* changes in response during cell cycle. *Mutation Res.*, 1967, *4*, 579–599.
45. Sinclair, W. K. Radiation effects on mammalian cell populations in vitro. In: Radiation Research. Edited by G. Silini. North-Holland Publishing Company, Amsterdam, 1967, pp. 607–631.
46. Sinclair, W. K. Cyclic x-ray responses in mammalian cells *in vitro*. *Radiation Res.*, 1968, *33*, 620–643.
47. Sinclair, W. K., and Morton, R. A. X-ray sensitivity during cell generation cycle of cultured Chinese hamster cells. *Radiation Res.*, 1966, *29*, 450–474.
48. Terasima, T., and Tolmach, L. J. Changes in x-ray sensitivity of HeLa cells during division cycle. *Nature*, 1961, *190*, 1210–1211.
49. Terasima, T., and Tolmach, L. J. Variations in several responses of HeLa cells to x-irradiation during division cycle. *Biophys. J.*, 1963, *3*, 11–33.
50. Till, J. E. Radiation effects on division cycle of mammalian cells *in vitro*. *Ann. New York Acad. Sc.*, 1961, *95*, 911–919.
51. Tolmach, L. J., Terasima, T., and Phillips, R. A. X-ray sensitivity changes during division cycle of HeLa S3 cells and anomalous cervical kinetics of developimg microcolonies. In: Cellular Radiation Biology. Williams & Wilkins Company, Baltimore, 1965, pp. 376–393.
52. Van Lancker, J. L. Cytochemical injury of x-radiation. *Fed. Proc.*, 1962, *21*, 1118–1123.
53. Weinbren, K. Regeneration of liver. *Gastroenterology*, 1959, *37*, 657–678.
54. Whitmore, G. F., Gulyas, S., and Botond, J. Radiation sensitivity throughout cell cycle and its relationship to recovery. In: Cellular Radiation Biology. Williams & Wilkins Company, Baltimore, 1965, pp. 423–441.
55. Whitmore, G. F., Gulyas, S., and Till, J. E. Radiation-induced mitotic delay in L cells. *Radiation Res.*, 1967, *30*, 155–171.
56. Wolff, S. Chromosome aberrations and cell cycle. *Radiation Res.*, 1968, *33*, 609–619.
57. Wolff, S. Radiation effects as measured by chromosome damage. In: Cellular Radiation Damage. Williams & Wilkins Company, Baltimore, 1965, pp. 167–183.
58. Wolff, S., and Luippold, H. E. Mitotic delay and apparent synergism of far red radiation and x-rays in production of chromosomal aberrations. *Photochem. & Photobiol.*, 1965, *4*, 439–446.
59. Yu, C. K., and Sinclair, W. Mitotic delay and chromosomal aberrations induced by x-rays in synchronized Chinese hamster cells *in vitro*. *J. Nat. Cancer Inst.*, 1967, *39*, 619–631.

PATTERNS OF PROTEIN SYNTHESIS IN THE HELA CANCER CELL*

By GERALD M. KOLODNY, M.D.†
BOSTON, MASSACHUSETTS

RADIOSENSITIVITY of a tissue depends to a great degree upon the radiosensitivity of its component cells. Cells which are dividing undergo a sequence of internal metabolic events beginning with one mitosis and concluding with the next. This sequence, termed the cell cycle, secures a duplication of all the cell constituents for the next cell division.

Radiosensitivity of a cell depends upon its position in the cell cycle. Terasima and Tolmach[16] demonstrated periods of relative radiosensitivity during mitosis and late G_1 and periods of relative radioresistance during early G_1 and late S. Sinclair,[14] in a recent review, refers to 6 different responses to radiation that vary with the position of the cell within the cell cycle. These are "survival, chromosome aberrations, division delay, modifications to DNA synthesis, incidence of small colony formation and extent to which cells attempt the first postirradiation division."

These changes in radiosensitivity during the cell cycle undoubtedly reflect intracellular changes in patterns of nucleic acid synthesis leading to changes in patterns of protein synthesis, or reflect changes in patterns of protein synthesis directly as the cell proceeds through its cell cycle.

There is some evidence that there is a change in the amount of some proteins that are present at different times in the cell cycle. Synchronized cultures of microorganisms show periodic increases in the activity of various enzymes. The synthetic bursts represented by such increases have been related by various models to sequences of transcription.[5,7,19] Enzyme activities in eukaryotic cells also change during the generative cycle. Activities of lactate dehydrogenase and of glucose-6-phosphate dehydrogenase increase intermittently through the cell cycle in cultured Chinese hamster cells,[8] suggesting that synthesis is itself intermittent, or that complex cycles of synthesis and degradation are the source of variation in activity. Histones of HeLa cells are synthesized in the cytoplasm, and this synthesis is coincident with the S phase, *i.e.*, DNA replication.[11]

In order to understand fully the mechanisms responsible for radiosensitivity and its variation during the cell cycle, we must know more about the whole pattern of cellular protein synthesis and how it varies as the cell goes through the cell cycle. How widespread are shifts in protein synthetic patterns among the very large population of proteins found in cells?

Experiments reported here were done in order to compare patterns of protein synthesis at various stages in the cell cycle. Proteins were labeled with leucine-H^3 or leucine-C^{14} during the G_2 period, during mitosis and during the entire cell cycle. Cells were obtained in mitosis by shaking them off monolayer cultures,[12] or in all stages of the cell cycle by scraping a monolayer culture off the glass surface upon which it was growing. Cells containing radioactive proteins were mixed as batch pairs and their soluble proteins extracted and separated by acrylamide gel electrophoresis. In each pair, proteins from different phases of the cell cycle, or in controls, from the same phase, were

* Presented at the Sixteenth Annual Meeting of the Association of University Radiologists, Columbus, Ohio, May 8–11, 1968.
From the Department of Radiology, Harvard Medical School, Massachusetts General Hospital, Boston, Massachusetts and the Department of Biology, Massachusetts Institute of Technology, Cambridge, Massachusetts.
Supported by Grants to Professor Paul R. Gross (M.I.T.) from the National Institutes of Health U.S.P.H.S. (GM-13560-03), the National Science Foundation (GB-5760), and the American Cancer Society (E-285).
† Advanced Academic Fellow of the James Picker Foundation; Postdoctoral Fellow of the Department of Biology, Massachusetts Institute of Technology; and Clinical Fellow of the Department of Radiology, Massachusetts General Hospital.

labeled with H^3 and C^{14} tracers. The gels were sliced and radioactivity in each slice was assayed by liquid scintillation spectrometry. In all cases, analysis of the radioactivity distributions revealed significant differences in pattern between different cell cycle phases, and no such differences between H^3- and C^{14}-labeled control pairs.

MATERIALS AND METHODS

CELLS AND MAINTENANCE

HeLa cells (S-3) with a 22 hour intermitotic time were maintained in spinner cultures at 37°C. in Joklik's modification of SMEM* with 10 per cent horse serum added. All transfers and manipulations were performed with prewarmed glassware and media, and the monolayer cultures were prepared in 32 ounce flint glass bottles,† washed in "7X"‡ and rinsed 10 times in deionized water.

M/I CELL MIXTURES

Monolayer cultures were prepared by transferring 40 ml. spinner culture (5×10^5 cells/ml.) into each of 20 bottles. Twelve hours later, 19 of the bottles were shaken to dislodge dead cells, mitotic cells, and debris, and fresh medium was added. The twentieth bottle was treated the same way 2 hours later, except that the replacing medium was MEM[2] lacking leucine and calcium, but with NaCl in sufficient amount to restore normal osmolarity, and containing 10 per cent horse serum. This is the I culture. The serum adds to the final solution about 2 mg./l. leucine,[18] which is about 1/25 the concentration in standard MEM.

At the same time (14 hours after the start of the experiment), the media in the 19 other bottles were poured off: 40 ml. of the medium deficient in Ca^{++} and leucine was added to one of them, and cells in mitosis were collected by gentle shaking.[12] The medium, now containing cells in M from the first bottle, was added to the second bottle, which was shaken, and then to the third, and so on. Mitotic cells from all 19 bottles were thus collected in 40 ml. of Ca^{++}-leucine deficient medium. This suspension was placed in a new culture bottle. At least 80 per cent of the cells were, by microscopic check, in mitosis. This is the M culture. The cell density was about 5.5×10^5 ml.$^{-1}$.

The I and M cultures were gassed with 5.0 per cent CO_2 in air. To the I culture, there were added 2 μc/ml. leucine-C^{14} (250 mc/mM.*), while the M culture was treated with 100 μc/ml. leucine-H^3 (5 c/mM*). Cultures were allowed to incorporate the radioactive leucine for 90 minutes at 37°C. Cells were then quickly removed from their bottles, with the aid of a rubber policeman, and transferred to 40 ml. of Earle's salt solution[4] at 4°C. The cells from each culture were collected by centrifugation at $1{,}600\times$ g for 2 minutes, and then washed 3 times with the same medium after mixing. The mixture of cells thus obtained consists of cells whose proteins, synthesized during mitosis, contain leucine-H^3, plus cells with proteins synthesized during all the rest of the cell cycle (I) and containing leucine-C^{14}.

G_2/(M+I) MIXTURES

Ten monolayer cultures were prepared as described above. The old media were discarded with gentle shaking, and fresh Ca^{++}-leucine deficient medium was added, together with leucine-H^3 at 36 μc/ml. The bottles were gassed with CO_2-air mixture and incubated at 37°C. for 120 minutes. Radioactive media were poured off very carefully, after cells in mitosis were harvested by shaking them into cold Earle's solution as described above. The celis collected in this way had received most of their exposure to labeled leucine during the late G_2 phase of their reproductive cycles and isolated while the cells were in mitosis. This is the G_2 population.

* Grand Island Biological Co., Grand Island, New York.
† Brockway Glass Co., Inc., Brockway, Pennsylvania.
‡ Linbro Chemical Co., New Haven, Connecticut.

* New England Nuclear Corporation.

(M+I) cells for this series were prepared as follows: Twelve hour monolayer cultures were very carefully freed of old medium and given fresh Ca^{++}-leucine deficient medium containing 2 μc/ml. leucine-C^{14}. Following 120 minutes of incubation, cells in mitosis were removed, along with the radioactive medium, by gentle rocking. Such cells had been exposed to the label mainly during their late G_2 phases. These cells were discarded. Some of the cells remaining attached to the glass were still in G_2 and had synthesized radioactive proteins in early G_2. The remaining cells were in all other stages of the cycle and had synthesized radioactive proteins during S, M, and G_1. This is the (M+I) population.

Cells were removed from the glass by scraping, and then combined with the G_2 cells. Centrifugation and washing of the cell mixture were as described above.

$(G_2)_m/(M+I)_m$ MIXTURES

Media with dead cells and debris were removed from 12 hour monolayer cultures. Added to the cultures was 40 ml. of fresh medium with 1/10th the normal concentration of leucine and 3 μc/ml. of leucine-C^{14} (250 mc/mM*).

After labeling all the cell proteins for 24 hours with leucine-C^{14} the medium was discarded with dead cells and debris and 40 ml. fresh leucine-free medium was added with 60 μc/ml. of leucine-H^3 (5 c/mM*). Two hours later mitotic cells were harvested from the bottles by gently rocking the media about 20 times.[12] At least 75 per cent of the cells were, by microscopic check, in mitosis. These cells had received their exposure to leucine-H^3 during the G_2 phase of their reproductive cycles. Their exposure to leucine-C^{14} occurred throughout their reproductive cycles. However, the cells were isolated in the same phase of the cell cycle during mitosis.

CONTROL CELL MIXTURES

Media were gently discarded from two 12 hour monolayer cultures. Ca^{++}-leucine deficient medium was then added to each (40 ml.). One received 2 μc/ml. leucine-C^{14}, while the other received 10 μc/ml. leucine-H^3. Both bottle cultures were incubated for 120 minutes, following which all cells were collected by scraping and washing. The cell mixture thus contained cells in mitosis plus interphase (M+I), labeled separately with H^3 and C^{14} in proteins synthesized at all stages of the cell cycle. The two populations of proteins thus mixed are identical except for the presence of leucine-H^3 in half of the proteins and of leucine-C^{14} in the identical other half.

PREPARATION OF PROTEINS FOR ELECTROPHORESIS

Cells from each of the 4 mixtures (M/I, G_2/(M+I), $(G_2)_m/(M+I)_m$, and M+I/M+I) were centrifuged and re-suspended in 4 ml. of the following hypotonic buffer: 0.01M NaCl; 0.01M tris (hydroxymethyl) aminomethane, pH 7.4; 0.0015M $MgCl_2$. Lysis was accelerated by pipetting or by the use of a Dounce homogenizer. The lysate was centrifuged at 10,000×g for 10 minutes, and the supernatant solution from this was then centrifuged for 1 hour at 105,000×g, 4°C.

The 105,000×g supernatants were dialyzed in the cold for 16 hours against electrophoresis buffer containing 8M urea. These dialyzates were used as samples for gel electrophoresis.

ELECTROPHORESIS

Polyacrylamide gels, and the procedures for their use in electrophoresis, were as described by Davis,[1] with slight modification. All solutions were made up with 8M urea, instead of H_2O, as solvent. This ensured that all species in what were expected to be very complex mixtures of proteins would remain in sub-unit form, and prevented aggregation during the dialysis and subsequent separation in the electric field. The buffer system was tris-glycine at pH 8.3. Running gels 85 mm. long, containing 5 per cent acrylamide,

* New England Nuclear Corporation.

were topped with spacer gels of 2.5 per cent concentration. The gels were set in 6 mm. inner diameter pyrex tubes. Samples were layered directly atop the spacer gels with the aid of a string dauber and pipette. Gel-containing tubes were placed in the electrophoresis chamber (designed by Mr. G. Fairbanks of this Department) and migration was allowed to proceed in the cold at currents of 2 ma./sample for 4 or 8 hours.

Gels were removed by rimming with a 22 gauge spinal needle while injecting water through the needle. The gels were stained with Amido Black in 7 per cent acetic acid, and then de-stained in the acid alone. These gels were used for examination of their bulk protein banding patterns.

Duplicate *unstained* gels were sliced transversely at 0.5 mm. thickness. These slices were cut from frozen gels with a transporting and chopping device designed by Loening.[9] Following a technique devised in this laboratory by Terman,[17] slices were placed singly or in adjacent pairs into scintillation vials and dispersed with 0.3 ml. NCS.* A toluene-scintillation solution (15 ml.) was then added to each vial. The toluene contained 4 g./l. PPO and 0.5 g./l. POPOP.

PROTEIN DEGRADATION

Leucine-C^{14} (0.03 μc/ml.) was added to spinner cultures (3×10^5 cells/ml.) containing either complete SMEM media with 10 per cent horse serum or media with 1/10th the normal concentration of leucine with 10 per cent horse serum. After 24 hours, the cultures were centrifuged, washed 2 times with media, and re-suspended in complete media with 10 per cent horse serum. Cell counts showed normal growth of cells. At intervals over the following 24 hours, 10 ml. samples of the spinner culture were taken.

TCA precipitates[13] of the lysed cells from each 10 ml. sample were plated on 0.45 μ pore size millipore filters.†

The filters were air-dried overnight in scintillation vials then 15 ml. of the above scintillation fluid was added to each vial and the vials counted. All vials had > 10,000 cpm.

COUNTING

Liquid scintillation spectrometry was done on Beckman LS-150 and LS-250 liquid scintillation counters equipped with circuitry for automatic quench correction. This refinement is essential for experiments of this sort: it corrects for inhomogeneities in gel slice properties and in gel solubility. All samples were counted for a time sufficiently long to reduce counting errors to less than 1 per cent. Counting data given in the figures and used for the calculations discussed below are all corrected for background and quenching.

RESULTS

The electrophoretic patterns were, as expected, very complex. A sample stained gel is shown in Figure 1. When simpler protein mixtures are separated under the same conditions as were used for these experiments, a small number of discrete band patterns is obtained. Thus, ribosomal proteins give stain patterns of approximately 30 bands, with low optical densities between the major peaks. "Soluble proteins" from HeLa cells produce, in contrast, such large numbers of bands that fine structure of the stain pattern is lost in the region near the mean electrophoretic mobility. The photograph does not do justice to the method; however, close inspection of the gels even in the region of maximum optical density reveals large numbers of sharp bands superimposed upon a distribution of moderate background density.

Four hour periods of electrophoresis resulted in migration of the fastest peaks to the end of the running gels: in this interval, most of the proteins remained in the upper (cathodal) third of the gel. When electrophoresis was allowed to continue for 8 hours, considerable amounts of

* Nuclear-Chicago Corporation.
† Millipore Corporation, Bedford, Massachusetts.

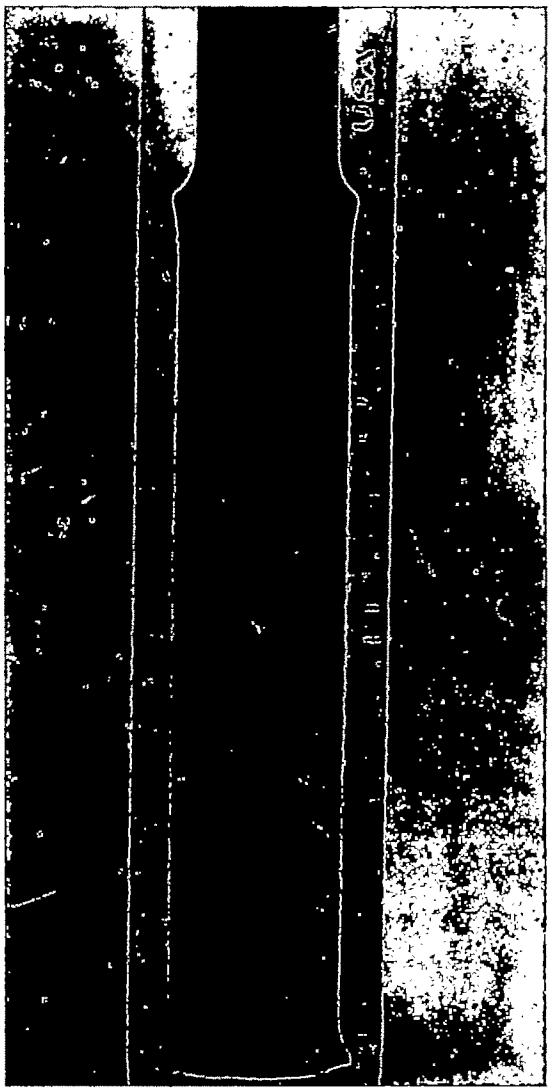


FIG. 1. Photograph in white light of a typical stained 4 hour gel. Details are in the text. Cathode and spacer gel are at the top.

protein moved off the anodal end of the running gel. Some fast-migrating species were then lost.

Radioactivity distributions were superficially like the optical density patterns, except that the fine structure of the protein distributions was more evident in them. A typical radioactivity distribution from the series here described is shown in Figure 2. This shows radioactivity in pairs of successive 0.5 mm. gel slices (*i.e.*, 70 fractions counted; 140 sliced). The sample mixture contained proteins labeled in G_2 with leucine-H^3 and proteins labeled in M and I with leucine-C^{14}. The pattern shown is from a 4 hour electrophoretic run.

Like this one, all other direct counts/min. patterns were complex and followed roughly the optical density patterns. The shapes of the H^3 and C^{14} distributions were also superficially alike. In order to analyze the distributions in more detail, and to express identities (or lack thereof) in the 2 isotope distributions quantitatively, the electrophoretic patterns were analyzed as follows:

The number of disintegrations/min. (dpm) was obtained for each isotope in each fraction and for each fraction a dpm ratio was computed. The mean value of all such ratios was then determined for a gel. The normalized ratio, ρ, was then obtained for each fraction by

$$\rho_i = \frac{(\text{dpm } H^3/\text{dpm } C^{14})_i}{(\text{dpm } H^3/\text{dpm } C^{14})_{\text{average}}} .$$

Values of these normalized ratios were plotted as a function of the fraction number (separation length along the gel, propor-

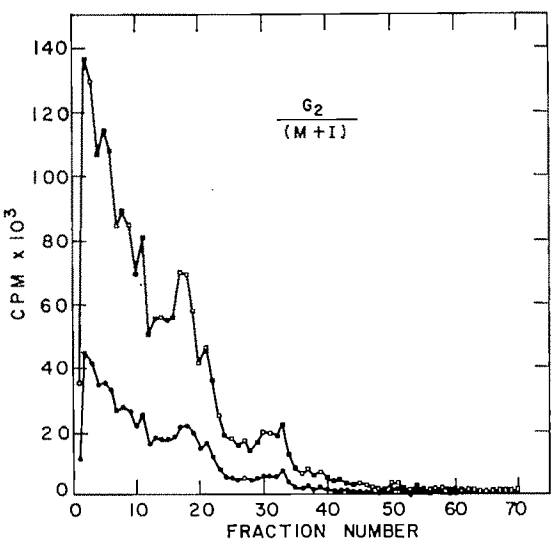


FIG. 2. Radioactivity distributions for proteins labeled with leucine-H^3 in G_2 and with leucine-C^{14} in (M+I). Squares=H^3. Circles=C^{14}. Each gel fraction contains two 0.5 mm. gel slices. Electrophoresis for 4 hours as described in the text.

tional to electrophoretic mobility).

Figure 3 shows a plot of such data obtained from the radioactivity distribution in Figure 2. It will be seen that deviations from unity in ρ are very large and occur everywhere in the gel. Recall that the protein populations being compared here were the G_2 and the (M+I). Such widespread fluctuations in the normalized isotope ratio would not, of course, be expected if the H^3- and C^{14}-labeled protein populations were identical. In order to test sensitivity and reproducibility of the method, several control sets of labeled proteins, identical except for their content of H^3 or C^{14}, were subjected to the same kind of analysis. A sample of one of these is shown in Figure 4, which represents the normalized ratios for the (M+I)/(M+I) control pair described earlier.

Deviations from unity in the normalized ratios were always very small in control runs. Figure 4 is a typical, rather than selected result. Some others were much better.

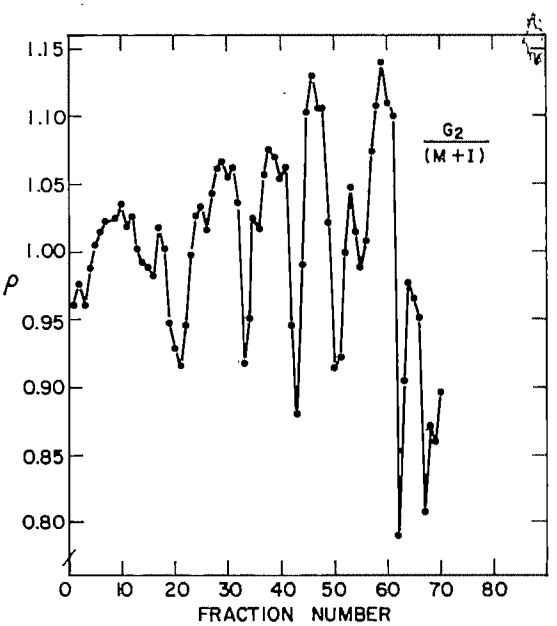


FIG. 3. The ρ, or normalized isotope ratios,

$$\frac{(\text{dpm } H^3/\text{dpm } C^{14})}{(\text{dpm } H^3/\text{dpm } C^{14})_{av.}},$$

for the electrophoretic pattern represented by the graph in Figure 2.

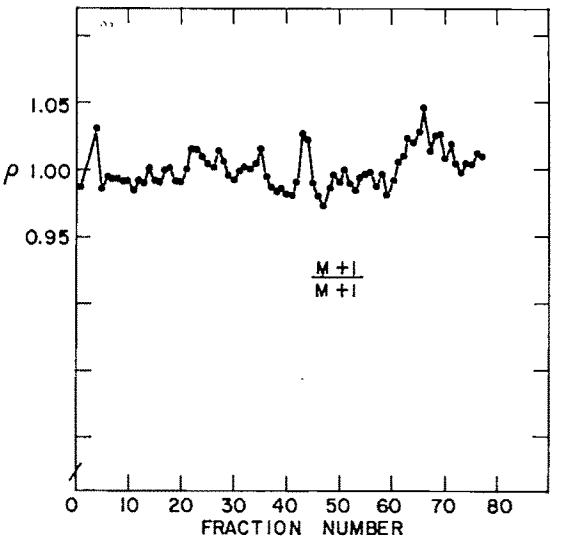


FIG. 4. Plot of ρ *vs.* fraction number for a control protein mixture;

$$\frac{(M+I)_{H^3}}{(M+I)_{C^{14}}}.$$

The pattern of normalized ratios for the pair M/I is shown in Figure 5. Deviations from unity are again quite large, but the pattern of those deviations is different

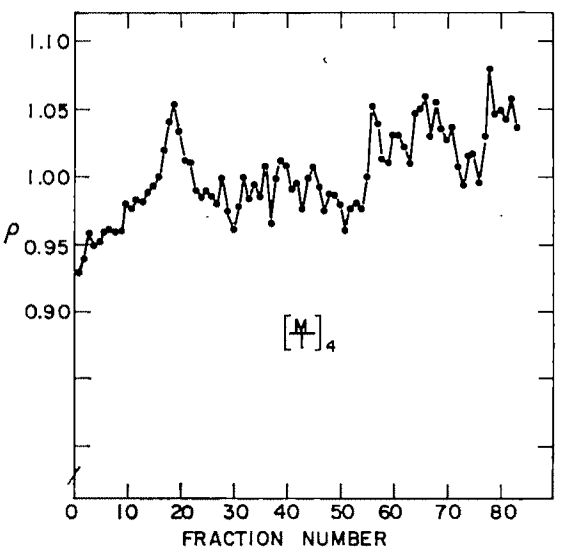


FIG. 5. Plot of ρ *vs.* fraction number for the M/I protein mixture. Details in the text. These data are from a 4 hour electrophoretic run.

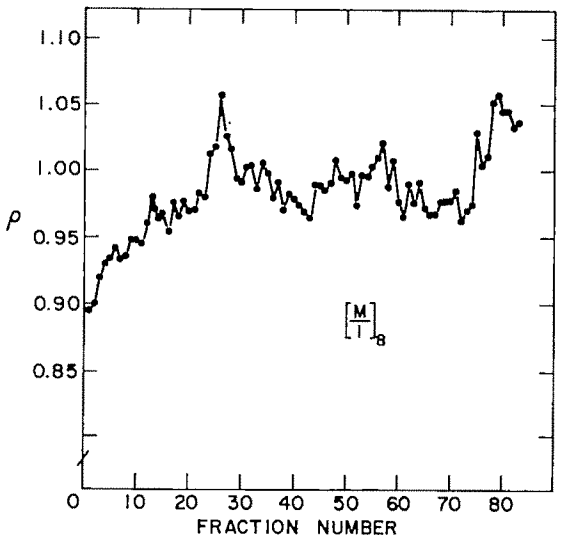


FIG. 6. Data are like those in Figure 5, except that electrophoresis was continued in this run for 8 hours.

from that seen in the $G_2/(M+I)$ gels. These ρ/fraction patterns are reproducible, from gel to gel and from experiment to experiment. In Figure 6 is shown, for example, the ρ/fraction pattern for a gel on which an M/I pair was run for 8 hours, instead of 4.

The ρ/fraction data are in a form that allows simple assessment of the significance of apparent differences between the members of a population pair. The variance of the ρ distribution about its mean can easily be computed, and the ratio of experimental pair variance to control pair variance gives a value of Snedecor's "F,"[15] from which probability values for the null hypothesis can be calculated, or obtained in tables. The results of a series of such calculations for the experimental runs described above are shown in Table 1. By the test used, the M/I and $G_2/(M+I)$ pairs are significantly different within each pair. The probability of the null hypothesis is in each case much less than 0.001. Also, the M/I and $G_2/(M+I)$ ρ distributions are visibly different from each other.

In both the M/I and the $G_2/(M+I)$ mixtures, the populations of proteins being compared have been isolated from cells at different stages of the cell cycle. The M cells were isolated in late mitosis and the I cells were isolated in all phases of interphase. The G_2 cells were isolated in mitosis and the M+I cells were isolated in all phases of interphase. Comparison of identically labeled proteins isolated from interphase cells and co-electrophoresed with those isolated from mitotic cells showed some differences in the extractability of different proteins at different stages of the cell cycle. This is not surprising since there are many structural changes in a cell as it proceeds through its cell cycle. These differences in extractability, however, could not account for the variations in ρ seen in Figures, 3, 5 and 6.

To eliminate the contribution of differences in extractability at different cell cycle stages, proteins labeled at different stages in the cell cycle were extracted from cells in the same stage of the cell cycle, during mitosis.

Figure 7 is a plot of ρ *vs.* fraction number for this $(G_2)_m/(M+I)_m$ protein mixture. Deviations in ρ are once again very large and occur throughout the gel. Here again

TABLE I*

CHANGES IN PROTEIN SYNTHETIC PATTERN DURING THE HeLa CELL CYCLE

Sample Mixture	Variance of ρ ($\sigma^2 \times 10^4$)	Variance Ratio (F)	P_{null}
(M+I)/(M+I) (control)	1.96	—	—
M/I	9.79	5.0	<0.001
$G_2/(M+I)$	14.3	25.5	<0.001

* The sample symbols and ρ are defined in the text. Variance (σ^2) refers to the variance of all ρ values in a gel, *i.e.*,

$$\sigma^2 = \frac{\Sigma (\rho - 1)^2}{\text{total fractions}}.$$

The value of Snedecor's F is therefore given by the ratio

σ^2 experimental/σ^2 control.

The probabilities are obtained from Snedecor's tables,[15] using appropriate degrees of freedom. The null hypothesis states that experimental ρ distributions do not differ significantly from the control ρ distribution. That hypothesis is rejected at the 0.001 probability level.

the probability of the null hypothesis is far less than 0.001.

These last experiments also eliminate the possibility that some variations in synthetic pattern may have been caused by labeling two separately growing populations of cells. In these experiments the same population of cells was labeled with both isotopes.

Any large amount of protein degradation that differed from protein to protein and cell stage to cell stage would be expected to influence the ρ values obtained. Protein degradation was measured over a 24 hour chase period after a 24 hour pulse with leucine-C^{14}. Figure 8 shows the decline in radioactivity over a 24 hour period. A regression equation for this plot was calculated by the method of "least-squares" and the slope was found to be less than 0.75 per cent per hour. This low level of protein degradation in HeLa cells is slightly less than the 1.0 per cent per hour found by Eagle *et al.*,[3] but probably greater than that seen in mouse fibroblasts.[19] This loss of protein, however, is too small to contribute significantly to the changes in ρ seen in the figures.

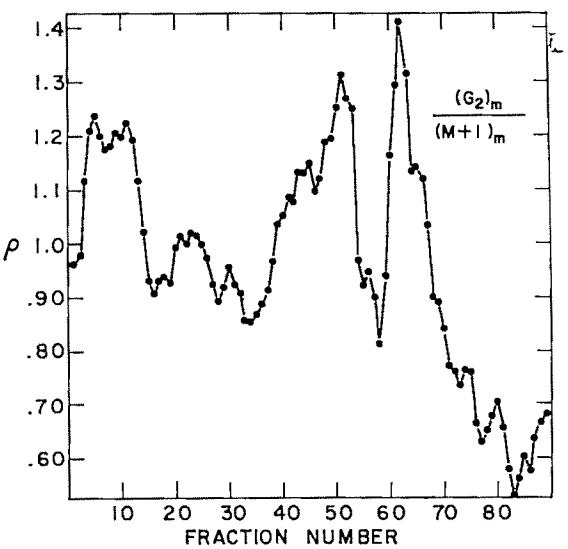


Fig. 7. Plot of ρ *vs.* fraction number for the $(G_2)_m/(M+I)_m$ mixture. All proteins extracted while cells in mitosis. Run was for 4 hours.

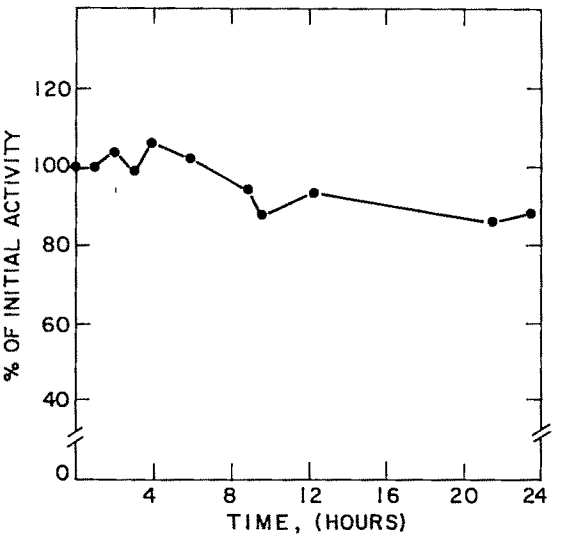


Fig. 8. Protein degradation. Random population of cells pulsed for 24 hours with leucine-C^{14} and chased for 24 hours with normal medium. Decline in radioactivity plotted as per cent of initial radioactivity over 24 hours.

DISCUSSION

The data show that changes in the over-all pattern of protein synthesis occur during the mammalian cell cycle. These changes are widespread throughout the whole spectrum of proteins synthesized by the HeLa cell.

The results do not permit conclusions about the source of variation in the radioactivity patterns. It could arise because there are different kinds of proteins being synthesized at the different stages. Data mentioned in the introduction indicate that this source of variation certainly plays a part. But the variation could equally well result from altered *rates* of synthesis among a large and constant set of proteins, and, in fact, that also must play some role, since enzyme and histone syntheses are not turned on and off as square waves. Electrophoretic patterns of a complexity such as is shown in the Figures represent hundreds (at least) of protein species. It is unlikely that any peak seen in the pattern contains only one species of polypeptide.

Cellular differentiation is the result of

progressive changes in the pattern of protein synthesis within the cell.[6] The results indicate that the sequence of events making up a single cell cycle is a primary example of differentiation. Further study on the controls responsible for these changes in protein synthetic patterns during the cell cycle should be helpful in understanding how differentiation is controlled.

Changes in protein synthetic pattern may be related to changes in radiosensitivity during the cell cycle. The above data, however, do not allow any firm conclusions to be drawn on this relationship. Further analysis and comparison of protein synthetic patterns during periods of relative radioresistance and radiosensitivity are necessary before any direct relationships may be found. Further work is now underway as well on prefractionation of the isolated proteins prior to electrophoresis.

SUMMARY

Variations in radiosensitivity occur during the cell cycle. In order to better understand the reasons for these variations, protein synthesis during the cell cycle has been studied. Proteins synthesized in one stage of the cell cycle have been labeled with one isotope and those proteins synthesized during other stages of the cell cycle labeled with a second isotope. The proteins so labeled were co-electrophoresed on polyacrylamide gels. The radioactivity distributions on the gels were analyzed and showed significant differences in the distributions of the two isotopes. Such differences indicate differences in the kinds of and/or rates of synthesis of proteins as the cell goes through the cell cycle. No definite correlation can yet be made between specific proteins or protein synthetic patterns and specific cell cycle changes in radiosensitivity. However, the fact that changes in the patterns of protein synthesis are here shown to exist suggests that further study of patterns of protein synthesis may lead to basic mechanisms of radiosensitivity.

Department of Radiology
Massachusetts General Hospital
Boston, Massachusetts 02114

The author thanks Professor Paul R. Gross, Department of Biology, Massachusetts Institute of Technology, for the use of his laboratory and his advice throughout these studies.

REFERENCES

1. Davis, B. J. Disc electrophoresis. II. Method application to human serum proteins. *Ann. New York Acad. Sc.*, 1964, *121*, 306, 650.
2. Eagle, H. Amino acid metabolism in mammalian cell cultures. *Science*, 1959, *130*, 432–437.
3. Eagle, H., Piez, K. A., Fleischman, R., and Oyama, V. I. Protein turnover in mammalian cell cultures. *J. Biol. Chem.*, 1959, *234*, 592–536.
4. Earle, W. R. Production of malignancy *in vitro*. IV. Mouse fibroblast cultures and changes seen in living cells. *J. Nat. Cancer Inst.*, 1943, *4*, 165–212.
5. Gorman, J., Taruo, P., LaBerge, M., and Halvorson, H. Timing of enzyme synthesis during synchronous division in yeast. *Biochem., Biophys. Res. Commun.*, 1964, *15*, 43–49.
6. Gross, P. R. The control of protein synthesis in embryonic development and differentiation. Topics in Devel. Biol. Edited by A. A. Moscona and A. Monroy. Academic Press, Inc., New York, 1967.
7. Kates, J. R., and Jones, R. F. Periodic increases in enzyme activity in synchronized cultures of Chlamydomonas Reinhardtii. *Biochim. et biophys. acta*, 1967, *145*, 153–158.
8. Klevecz, R. R., and Ruddle, F. H. Cyclic changes in enzyme activity in synchronized mammalian cell cultures. *Science*, 1968, *159*, 634–636.
9. Loening, U. E. Fractionation of high-molecular-weight ribonucleic acid by polyacrylamide gel electrophoresis. *Biochem. J.*, 1967, *102*, 251–257.
10. Masters, M., Kuempel, P. L., and Pardee, A. B. Enzyme synthesis in synchronous cultures of bacteria. *Biochem., Biophys. Res. Commun.*, 1964, *15*, 38–42.
11. Robbins, E., and Borun, T. W. Cytoplasmic synthesis of histones in HeLa cells and its temporal relationship to DNA replication. *Proc. Nat. Acad. Sc.*, 1967, *57*, 490–516.
12. Robbins, E., and Marcus, P. I. Mitotically synchronized mammalian cells: simple method for obtaining large populations. *Science*, 1964, *144*, 1152–1153.
13. Siekevitz, P. Uptake of radioactive alanine *in vitro* into proteins of rat liver fractions. *J. Biol. Chem.*, 1952, *195*, 549–565.
14. Sinclair, W. K. Cyclic x-ray responses *in vitro*. *Radiation Res.*, 1968, *33*, 620–643.
15. Snedecor, G. W. Statistical Methods Applied

to Experiments in Agriculture and Biology. Fifth edition. State College Press, Iowa, 1957.
16. Terasima, T., and Tolmach, L. J. Changes in x-ray sensitivity of HeLa cells during division cycle. *Nature*, 1961, *190*, 1210–1211.
17. Terman, S. A. To be published.
18. Westfall, B. B., Peppers, E. V., Sanford, K. K., and Earle, W. R. Amino acid content of ultrafiltrate from horse serum. *J. Nat. Cancer Inst.*, 1954, *15*, 27–35.
19. Zetterberg, A. Protein migration between cytoplasm and cell nucleus during interphase in mouse fibroblasts *in vitro*. *Exp. Cell Res.*, 1966, *43*, 526–536.

ROENTGENOLOGIC STUDIES OF CEREBROSPINAL FLUID FORMATION IN THE DOG*

By D. GORDON POTTS, M.D., *and* RICHARD M. BERGLAND, M.D.
NEW YORK, NEW YORK

THERE is still no completely satisfactory method of measuring the rate of cerebrospinal fluid formation in man in health or disease. The methods of Lunn[8] and Masserman[9] suggest that approximately 430 ml. of cerebrospinal fluid is formed by man in 24 hours and if these estimates are correct, the cerebrospinal fluid remains one of the largest volumes of fluid formed by man that cannot be measured accurately.

METHODS OF MEASUREMENT

Present methods of measuring the rate of cerebrospinal fluid production are:

A. *Subarachnoid Drainage:*

(1) Riser[14] placed a cannula in the cisterna magna of a dog and found that in the first hour 10–20 ml. of cerebrospinal fluid was collected, and that after the second half-hour the rate of collection settled down to an average rate of 30 ml. in 24 hours. This was thought to be the rate of cerebrospinal fluid formation.

(2) Masserman[9] removed 20 ml. of cerebrospinal fluid in human subjects and noted the time taken for the cerebrospinal fluid pressure to return to approximately the original level. The pressure usually became stable at a level lower than the original. Lunn[8] used a very similar method.

(3) In his experiments on the effects of cerebral metabolism, Bering[1] allowed the cerebrospinal fluid of dogs to flow from the cisterna magna at a pressure 50 mm. below the right heart level with the dog lying on its right side.

All of these techniques of subarachnoid drainage are open to the following criticisms:

(1) The methods do not allow for the vascular compensation of the initial lowering of pressure.[10]

(2) In all of these studies the cerebrospinal fluid pressure is lowered and this may cause an increased exudation of cerebrospinal fluid.[3]

(3) Presumably some cerebrospinal fluid is being absorbed in the usual way while these observations are being made.

B. *Drainage from the Aqueduct:*

Flexner and Winters[6] placed a cannula in the aqueduct of a cat and the cannula was surrounded by an inflated balloon to prevent leakage. About 15 ml. of fluid was formed in a day (this method excludes the fluid formed in the fourth ventricle). The technique is not suitable for application to man except possibly on rare occasions when it could be performed at the time of posterior fossa surgery.

C. *Clearance of Injected Substances:*

A substance that is unlikely to diffuse into the brain tissue or into the blood vessels of the pia mater is introduced into the cerebrospinal fluid in known quantity. The rate of cerebrospinal fluid absorption can be estimated either from the rate of fall in concentration in the cerebrospinal fluid, or the rate of its appearance in the urine.

Phenolsulphonphthalein, inulin and dextran have been used in this way. Phenolsulphonphthalein is unsatisfactory because

* Presented at the Sixteenth Annual Meeting of the Association of University Radiologists, Columbus, Ohio, May 8–11, 1968.
From the Department of Radiology and the Department of Surgery (Neurosurgery), The New York Hospital–Cornell Medical Center, New York, New York.
Supported in part by USPHS General Research Support Grant No. 5-SOL-FR-05396-06.

there are modes of egress other than via the arachnoidal villi. Davson, Kleeman and Levin[4] found the fall in concentration of inulin to be about 17 per cent in 1 hour. This corresponded with a drainage rate of 0.3 per cent per minute.

The main objection to this type of technique is that the results are expressed as a fraction of the total volume of cerebrospinal fluid, which cannot be measured accurately in man during life.

D. *Rate of Turnover of Na^{24}:*

If a constant level of Na^{24} is maintained in the blood plasma, the rate of increase of activity in the cerebrospinal fluid will depend on 2 main processes:

(1) The appearance in the ventricles of newly-formed fluid with a concentration of Na^{24} approximately equal to that in plasma water.
(2) Diffusion to or from the adjacent parenchyma unaccompanied by fluid movements.

Probably the second of these processes is small and can be ignored because Na^{24} penetrates into the cerebrospinal fluid or brain tissue at almost the same rate. However, in this technique also, the results are expressed as a fraction of the total cerebrospinal fluid.

E. *Ventriculocisternal Perfusion:*

The technique of ventriculocisternal perfusion was developed by Pappenheimer *et al.*[12] and this method seems to provide the most satisfactory measurement of the rate of cerebrospinal fluid formation in animals that has been developed so far. Chronically prepared, unanesthetized goats were perfused from the lateral ventricle to the cisterna magna with artificial cerebrospinal fluid containing a known concentration of inulin or dextran. The dilution of the inulin or dextran gave a measure of the rate of formation of cerebrospinal fluid:

$$(Kx + Kf)Cout = Kx\,Cin$$

or

$$Kf = Kx\frac{(Cin\text{-}Cout)}{Cout},$$

where

Cin is the concentration in inflowing fluid.
$Cout$ is the concentration in outflowing fluid.
Kx is the rate of perfusion.
Kf is the rate of production of cerebrospinal fluid.

Although this method appears to give an accurate measurement of the rate of cerebrospinal fluid formation in animals, it is unlikely to be suitable for man except possibly when a cannula must be introduced into the lateral ventricle for other reasons.[15]

It therefore appears that the methods so far used for the measurement of the rate of cerebrospinal fluid formation are either inaccurate or unsuitable for use in man.

When patients being examined by pneumoencephalography or ventriculography are placed in the supine or "brow-up" position with air in the frontal horns and anterior portions of the bodies of the lateral ventricles, air will gradually disappear from the lateral ventricles, and the air-fluid levels in the bodies of the lateral ventricles will gradually move forward towards the foramen of Monro. In the past it has been presumed by most workers that this change in the air-fluid levels is due to air absorption. However, if we consider the fluid in the dependent portions of the lateral ventricles, presumably if the fluid level is gradually moving anteriorly and the quantity of fluid in each lateral ventricle remains constant, we must postulate that the fluid-filled portions of the lateral ventricles are gradually shrinking in size. Since the portions of the ventricular system outlined by air during these observations appear to remain constant in size, it seems rather unlikely that the fluid-filled portions would be diminishing. The changes observed in these fluid levels might therefore be better explained by the accumulation of cerebrospinal fluid in the lateral ventricles during

the period of observation. The quantity of cerebrospinal fluid thought to be formed by man is of the order of 15–20 ml. in 1 hour and it seems likely that the majority of this fluid is formed in the lateral ventricles. The average total volume of the ventricular system deduced from casts by Last and Tompsett[7] is about 22.4 ml. and therefore it is apparent that in 1 hour a quantity of fluid is formed in the ventricles sufficient to replace a significant fraction of the fluid in the ventricular system. When the lateral ventricles are small this evidence suggests that the volume of cerebrospinal fluid formed in the lateral ventricle in 1 hour could exceed the volume of the lateral ventricles. It would therefore be expected that, in patients with average or small lateral ventricles examined by pneumography and observed for a period of 30–60 minutes, cerebrospinal fluid formed during the period of observation should cause changes in the air-fluid levels. With the patient supine, the air-fluid level in the body of the lateral ventricle would be expected to move anteriorly as fluid accumulates in the lateral ventricle. The changes one would predict to be caused by fluid formation therefore seem to correspond with those observed in patients.

It has been shown[13] in patients undergoing cerebral pneumography that fluid accumulates in the air-filled temporal horn with the patient in the prone position. The changes observed during these studies could not be caused by air absorption. They could only be caused by the accumulation of fluid in the temporal horn during the period of observation.

Experiments were carried out on dogs to determine whether the formation of cerebrospinal fluid could be demonstrated by ventricular studies. Mongrel dogs weighing 30–48 pounds were anesthetized with sodium pentobarbital and burr holes were placed in the posterior parietal regions bilaterally.

EXPERIMENTS WITH LIPIODOL ASCENDANT

Lipiodol ascendant* is an oily contrast material which contains 10 per cent iodine and has a specific gravity less than that of cerebrospinal fluid, and when introduced into the ventricles it floats on the surface of the cerebrospinal fluid. Therefore, when it is introduced into the ventricular system, it is related to the cerebrospinal fluid in the ventricles in the same way as air, but it is not significantly compressed by changes in the intraventricular pressure and is not absorbed.

In 3 dogs, 1–1.5 ml. of lipiodol ascendant was introduced into the lateral ventricle on one side by puncture of one lateral ventricle. The contrast material passed into the third ventricle, aqueduct and fourth ventricle. In 1 case the third ventricle was punctured and lipiodol ascendant was introduced. The contrast material did not pass into the opposite lateral ventricle. The dogs were maintained in the supine or "brow-up" position for 60–90 minutes after introduction of the contrast material, and lateral roentgenograms were obtained at intervals of 10–20 minutes. Frontal roentgenograms were also taken at the beginning of the period of observation and at irregular intervals thereafter. The typical changes observed during the period of observation are illustrated in a dog where the third ventricle was punctured (Fig. 1, *A-D*). The initial roentgenogram (0 min.) (Fig. 1*A*) shows contrast material in the lateral ventricle, third ventricle, aqueduct and fourth ventricle. By 25 minutes (Fig. 1*B*), some fluid is shown accumulating in the suprapineal recess of the third ventricle and there is increased filling of the anterior extension of the lateral ventricle, presumably due to an increase in the pressure within the lateral ventricle due to the formation of fluid within the ventricle. These changes are more evident by 53 minutes (Fig. 1*C*); by 82 minutes (Fig. 1*D*) the posterior aspect of the contrast material in the lateral ventricle has moved anteriorly and the aqueduct and upper portion of the fourth ventricle no longer contain contrast material, which has been replaced by cerebrospinal fluid formation. Contrast material is now shown in the vallecula.

* E. Fougera and Company.

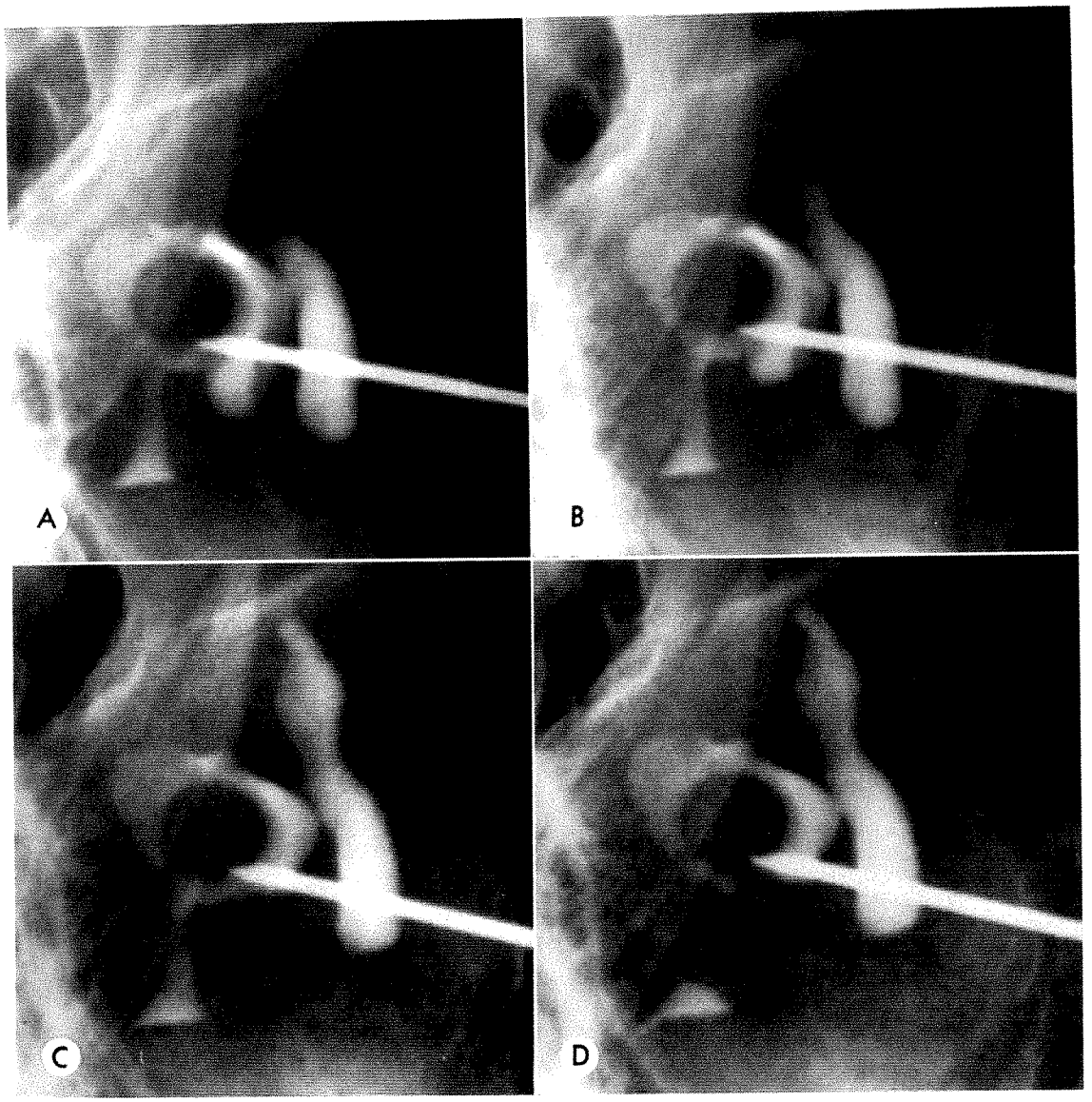


Fig. 1. (*A*) At 0 minutes lipiodol ascendant is shown in the lateral ventricle, third ventricle, aqueduct and fourth ventricle. (*B*) At 25 minutes the lateral ventricle is filled further anteriorly and the posterior portion of the suprapineal recess of the third ventricle is no longer opacified. (*C*) At 53 minutes the posterior aspect of the contrast material has moved anteriorly and the suprapineal recess is completely filled with cerebrospinal fluid. (*D*) At 82 minutes there is cerebrospinal fluid in the back of the third ventricle, in the aqueduct and upper fourth ventricle.

Experiments with air and pantopaque

In 10 dogs the cerebrospinal fluid in one lateral ventricle was replaced as completely as possible with air above and pantopaque (iophendylate injection U.S.P.) below with the dog in the supine or "brow-up" position. In every animal included in this study air passed into the opposite lateral ventricle and into the third ventricle, and the initial fluid levels in both lateral ventricles and the third ventricle were at least a few millimeters behind the foramen of Monro. Lateral roentgenograms were taken at intervals of 5–20 minutes.

In every dog (Fig. 2 and 3) there was a progressive accumulation of fluid of water density, presumably cerebrospinal fluid, between the air and the oily contrast mater-

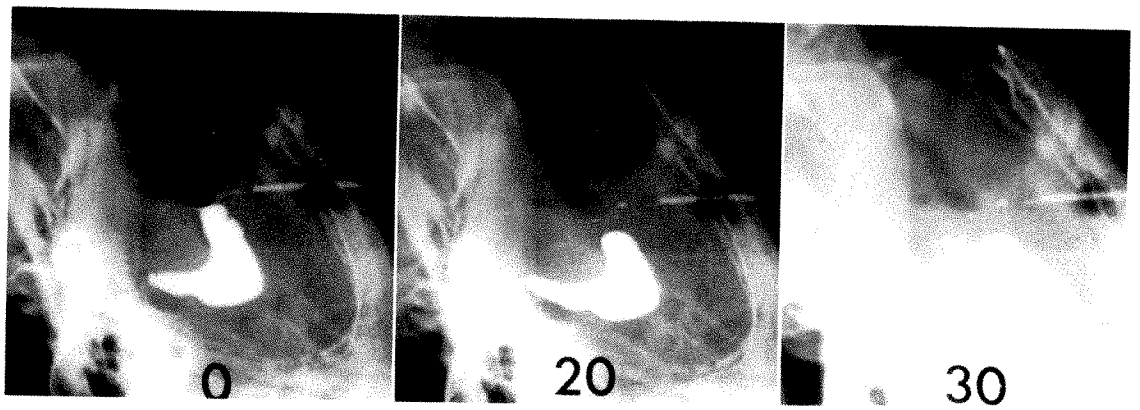


Fig. 2. Lateral roentgenograms at 0, 20 and 30 minutes showing the accumulation of cerebrospinal fluid between air and pantopaque. A small quantity of pantopaque is suspended on the newly formed cerebrospinal fluid by surface tension and indicates the upper aspect of the cerebrospinal fluid.

ial. In 5 dogs the cross-sectional area of the lateral ventricle was measured tomographically and corrected for magnification, and the corrected length of the column of fluid formed was measured to estimate the quantity of cerebrospinal fluid formed during the period of observation. The volume of fluid formed in one lateral ventricle was then calculated (Table 1).

Experiments with Pantopaque and Lipiodol Ascendant

It was hoped that by replacing most of the cerebrospinal fluid in the ventricles with

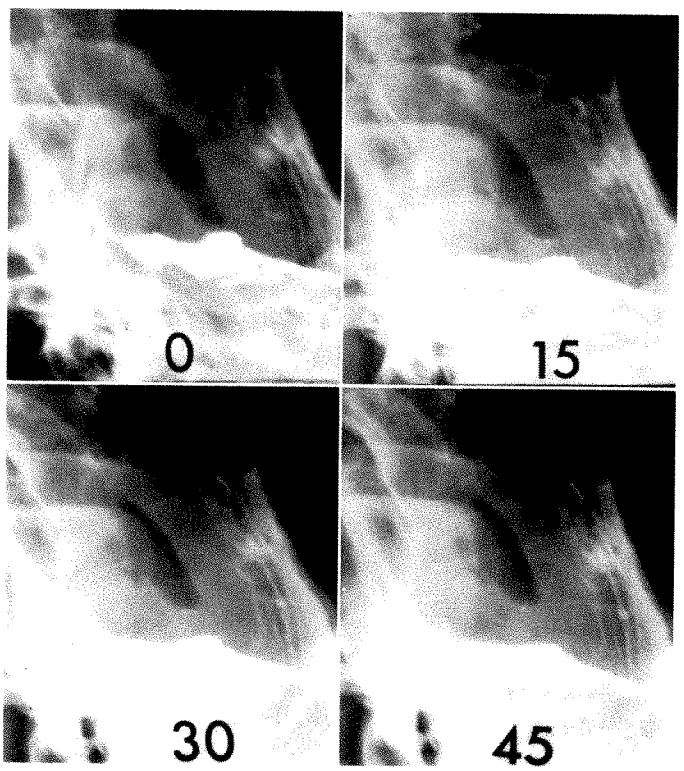


Fig. 3. Lateral roentgenograms at 0, 15, 30 and 45 minutes showing the accumulation of cerebrospinal fluid between air and pantopaque.

pantopaque and lipiodol ascendant it would be possible to observe the formation of cerebrospinal fluid between the two types of oily contrast material, one with a specific gravity higher than cerebrospinal fluid (pantopaque) and one with a specific gravity lower than that of cerebrospinal fluid (lipiodol ascendant). Unfortunately, the cerebrospinal fluid formed between the two types of contrast material did not separate into a well defined layer and there was some mixing of the two types of contrast material (Fig. 4, *A* and *B*). The method was therefore abandoned.

Table I

CEREBROSPINAL FLUID FORMATION

Dog No.	Cerebrospinal Fluid Formed in 1 Lateral Ventricle in 1 Hour (cc.)
1	0.13
2	0.21
3	0.12
4	0.18
5	0.14

DISCUSSION

The technique using lipiodol ascendant is similar to the technique used by De Rougemont and his collaborators,[5] who collected, under oil, the fluid freshly secreted by the choroid plexus of an opened lateral ventricle of the cat. The roentgenographic changes observed in the present study are very similar to the changes observed in patients undergoing cerebral pneumography. This provides good evidence that at least some of the changes seen in a patient undergoing cerebral pneumography and observed in the supine position for 30–60 minutes are due to cerebrospinal fluid formation.

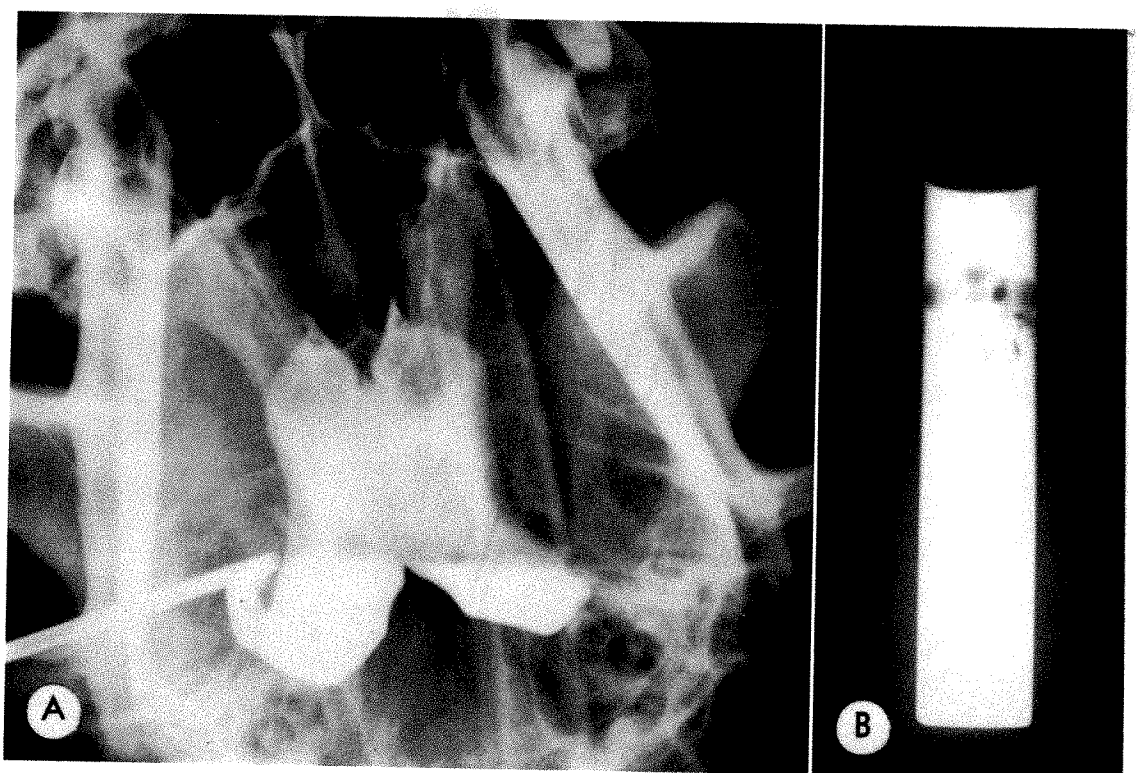


Fig. 4. (*A*) Horizontal ray base view showing lipiodol ascendant in the upper portions and pantopaque in the lower portions of the lateral ventricles. Round droplets of cerebrospinal fluid are seen between the two types of contrast material. (*B*) Roentgenogram of test-tube containing cerebrospinal fluid, pantopaque and lipiodol ascendant. The cerebrospinal fluid forms an irregular collection of droplets between the two types of contrast material.

The cerebrospinal fluid formed between air and pantopaque has been quantitated (Table 1) and it is found that fluid is collected in each lateral ventricle at the rate of 0.12–0.21 ml. per hour. The combined production of the two lateral ventricles is, therefore, 0.24–0.42 ml. per hour. Bering and Sato[2] have suggested that only one-third of the total cerebrospinal fluid produced by a dog is formed in the two lateral ventricles and third ventricle combined. There is no reliable estimate of the fraction produced by the lateral ventricles alone. Oppelt *et al.*[11] have shown that a dog forms about 50μl. of cerebrospinal fluid per minute or 3 ml. per hour. If only one-third of this (or 1 ml.) is produced by the lateral ventricles and third ventricle combined, the results obtained by roentgenographic methods seem consistent with results obtained by other methods. It is possible that air or contrast material in the ventricles or subarachnoid spaces may alter the rate of cerebrospinal fluid formation and this will require further investigation.

CONCLUSION

The observations made during these studies indicate that cerebrospinal fluid is formed in the ventricles of dogs, even when air, pantopaque or lipiodol ascendant are introduced into the ventricles. The experiments suggest the possibility of using roentgenographic ventricular studies for the estimation of the rate of cerebrospinal fluid formation in man.

SUMMARY

The formation of cerebrospinal fluid in dogs has been demonstrated by outlining the ventricles with lipiodol ascendant and with a combination of air and pantopaque. Using the latter technique, the fluid production estimated to be produced by two lateral ventricles was 0.24–0.42 ml. per hour.

D. Gordon Potts, M.D.
Department of Radiology
The New York Hospital—
Cornell Medical Center
525 East 68th Street
New York, New York 10021

We would like to thank Mr. Vishnu Deonarine, Mr. Salvatore Latterie and Mr. Robert Leshner for their help in this work.

REFERENCES

1. Bering, E. A., Jr. Cerebrospinal fluid production and its relationship to cerebral metabolism and cerebral blood flow. *Am. J. Physiol.*, 1959, *197*, 825–828.
2. Bering, E. A., Jr., and Sato, O. Hydrocephalus: changes in formation and absorption of cerebrospinal fluid within cerebral ventricles. *J. Neurosurg.*, 1963, *20*, 1050–1063.
3. Davson, H. Physiology of the Cerebrospinal Fluid. Little, Brown & Company, Boston, 1967.
4. Davson, H., Kleeman, C. R., and Levin, E. Quantitative studies of passage of different substances out of cerebrospinal fluid. *J. Physiol.*, 1962, *161*, 126–142.
5. DeRougemont, J., Ames, A., III, Nesbett, F. B., and Hofmann, H. F. Fluid formed by choroid plexus: technique for its collection and comparison of its electrolyte composition with serum and cisternal fluids. *J. Neurophysiol.*, 1960, *23*, 485–495.
6. Flexner, L. B., and Winters, H. Rate of formation of cerebrospinal fluid in etherized cats. *Am. J. Physiol.*, 1932, *101*, 697–710.
7. Last, R. J., and Tompsett, D. H. Casts of cerebral ventricles. *Brit. J. Surg.*, 1953, *40*, 525–543.
8. Lunn, V. Nogle undersogelser over spinalvaedskens hydromekanik. *Nord. med.*, 1945, *25*, 710–714.
9. Masserman, J. H. Cerebrospinal hydrodynamics. IV. Clinical and experimental studies. *Arch. Neurol. & Psychiat.*, 1934, *32*, 523–553.
10. Merritt, H. H., and Fremont-Smith, F. The Cerebrospinal Fluid. W. B. Saunders Company, Philadelphia, 1937.
11. Oppelt, W. W., Patlak, C. S., and Rall, D. P. Effect of certain drugs on cerebrospinal fluid production in dog. *Am. J. Physiol.*, 1964, *206*, 247–250.
12. Pappenheimer, J. R., Heisey, S. R., Jordan, E. F., and Downer, J. De C. Perfusion of cerebral ventricular system in unanesthetized goats. *Am. J. Physiol.*, 1962, *203*, 763–774.
13. Potts, D. G. Measurement of net rate of cerebrospinal fluid formation in portion of human lateral ventricle. *Radiology*, 1967, *89*, 1093–1095.
14. Riser, M. Le Liquide Cephalo-Rachidien. Masson et Cie, Paris, 1929.
15. Rubin, R. C., Henderson, E. S., Ommaya, A. K., Walker, M. D., and Rall, D. P. Production of cerebrospinal fluid in man and its modification by acetazolamide. *J. Neurosurg.*, 1966, *25*, 430–436.

Vol. 105. No. 4

LIPID EMBOLISM TO THE BRAIN FOLLOWING LYMPHOGRAPHY*

CASE REPORT AND EXPERIMENTAL STUDY

By J. W. DAVIDSON, M.B.†
TORONTO, ONTARIO, CANADA

ALTHOUGH deposition of ultrafluid lipiodol in the vascular bed of the lung occurs in all patients following diagnostic lymphography,[4–6,15] escape of the oily contrast medium to the systemic circulation, in quantities sufficient to cause clinical upset, is a rare event.[14] It has been shown in animals that the lung is an extremely effective filter for ultrafluid lipiodol,[9,18] and the rarity of cerebral complications of lymphography in man[12,14] is good evidence of a filtration mechanism. The purpose of this communication is to describe the case history of a patient with Hodgkin's disease in whom lipid embolization to the brain occurred within a few hours of lymphography performed after commencement of radiotherapy to the chest, and the results of a preliminary experiment on rabbits to test the hypothesis that radiation may have an immediate effect on the filtration mechanism for ultrafluid lipiodol in the lung.

REPORT OF A CASE

M. V., a 52 year old female, presented in October, 1965, with slight dysphagia and weight loss. A history of nonproductive cough for several weeks was elicited. No abnormality was present on clinical examination. Barium study of the gastrointestinal tract was normal, but on chest roentgenograms bilateral hilar lymphadenopathy was noted.

In view of progressive weight loss from her normal 132 pounds to 89 pounds, she was admitted to hospital in July, 1966. Mediastinoscopy showed slightly enlarged upper mediastinal lymph nodes which on biopsy and histologic examination were found to be infiltrated with typical Hodgkin's paragranuloma. An esophagogram at this time showed anterior extrinsic indentation of the esophagus at subcarinal level due to further lymphadenopathy, and tomography confirmed this finding in addition to delineating small lymph nodes in both lung hili. Bromosulphonphthalein test was abnormal showing 15 per cent retention at 45 minutes. Cephalin cholesterol flocculation was negative, and normal serum proteins, bilirubin, and SGOT were found. Electrocardiography, peripheral blood cell counts, and sternal marrow examination were normal.

On August 21, 1966, following transfer to this hospital, physical examination revealed a tired looking woman showing signs of recent weight loss. Small lymph nodes less than 1 cm. in size were palpable in both supraclavicular fossae. No further clinical evidence of lymphadenopathy was elicited and examination of the chest, central nervous system, and abdomen revealed normal findings apart from splenomegaly to 2 cm. below the costal margin.

Chest roentgenography prior to commencement of radiotherapy confirmed some enlargement of the soft tissues in the right perihilar region. Normal roentgenographic appearances of the lung fields, mediastinal shadow, and cardiac silhouette were demonstrated (Fig. 1). The time relationship of diagnostic lymphography and radiotherapy is illustrated on the inset of Figure 1. On August 25, 1966, cobalt 60 irradiation to the anterior chest and mediastinum was commenced with a dose of 100 rads at 6 cm. Lymphography was performed the following morning, 7 cc. of ultrafluid lipiodol being introduced into a subcutaneous lymphatic vessel on the dorsum of each foot over a period of 2 hours. Roentgenographic monitoring during introduction of the contrast medium showed normal flow in the lymphatics of the thighs,

* Based on the paper presented at the Sixteenth Annual Meeting of the Association of University Radiologists, Columbus, Ohio, May 8–11, 1968.
This work was supported in part by Grant 41-15 from The Ontario Cancer Treatment and Research Foundation.
† Senior Consultant in Diagnostic Radiology, The Ontario Cancer Institute; Assistant Professor in Diagnostic Radiology, University of Toronto, Toronto, Ontario, Canada.

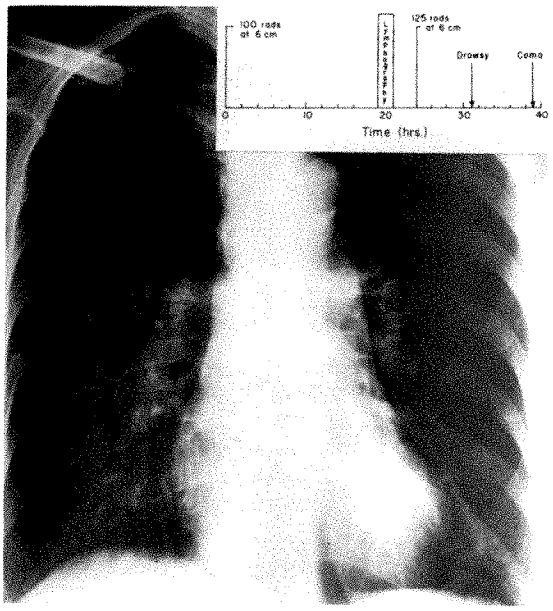


Fig. 1. Chest roentgenogram showing slight increase in the right perihilar soft tissues. Inset: Time relationship of radiotherapy and lymphography (Co^{60} teletherapy, SSD 130 cm., anterior field).

inguinal, iliac and para-aortic regions. Post injection roentgenograms revealed no evidence of lymphatic obstruction (Fig. 2), and only faint delineation of the thoracic duct was demonstrated. On completion of the lymphangiography, the patient appeared in good health and was returned to her cubicle. A further 125 rads of cobalt 60 irradiation to the mediastinum and middle thirds of the lung fields was given $2\frac{1}{2}$ hours following lymphography.

Eight hours later, the patient appeared drowsy and confused. Blood pressure was 80/60 mm. Hg, but no abnormal physical findings were elicited. She became gradually more confused and stuporous during the ensuing 12 hours, and remained in a comatose and unresponsive state. The pupils reacted to light and the optic fundi were normal. The motor power of the arms and legs appeared intact with withdrawal on painful stimuli, but generalized hypotonia was present. The tendon reflexes were diminished. The clinical examination of the chest and abdomen revealed no evidence of abnormality.

On the chest roentgenogram 20 hours following lymphography, a slight increase in interstitial markings in the lower zones of both lungs was noted, but no evidence of the characteristic stippled picture of ultrafluid lipiodol deposition was seen in the lung fields. As the patient was unconscious, roentgenography of the skull was undertaken, and numerous small opacities of contrast material density were revealed within the cranium on the right side. These were most obvious in the Towne's projection (Fig. 3) and on magnification consisted of a localized collection of radiopaque dots, several of which showed an arborizing pattern suggesting an intravascular location. Single anteroposterior roentgenogram of the abdomen showed opacified para-aortic lymph nodes of normal size, and at this time, routine oblique and localized projections were omitted due to the poor condition of the patient.

Progress. Treatment with parenteral fluids, hydrocortisone, and heparin was commenced and improvement in the level of consciousness occurred over the next 4 days. On September 1, 1966, she was able to recognize her husband and showed response to questioning. It was noted that serum calcium fell from 9.5 mg. to 7.7 mg. per cent on August 30th with a gradual return to normal. Serum biochemistry was normal. Cerebrospinal fluid protein was 82 mg.

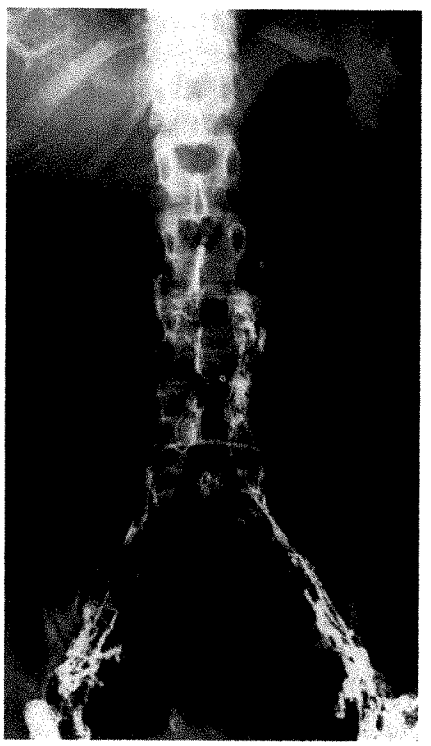


Fig. 2. Lymphangiogram showing normal flow.

per cent. Urine showed a growth of *E. coli* which responded to nitrofurantoin.

The patient was discharged on September 24, 1966, in good condition apart from retrospective amnesia and muscular hypotonia. The cobalt 60 irradiation course had been completed to 24 treatments in 4 weeks giving a tumor dose of 2,807 rads to the chest, and 3,500 rads to the midline at 6 cm. Review after 1 month showed improvement in her general condition and a further course of 3,400 rads of cobalt 60 irradiation to the abdomen was given. The neurologic examination was normal apart from slightly diminished muscle power. The calculating ability showed a "superior capacity." Slight slurring of speech was present.

After 6 months of relatively good health, gastrointestinal upset and generalized weakness were again noted. Hepatomegaly was present with abnormal liver function tests. Liver scan showed multiple small space-occupying lesions. Further treatment with cyclophosphamide, vincristine, and methylhydrazine was completed. Generalized weakness and anemia continued despite blood transfusion, oral prednisone, and velbe. Her general condition continued to deteriorate until death on August 15, 1967. Permission for autopsy was refused, but the clinical course was consistent with progressive Hodgkin's disease.

COMMENT

In the presence of normal intralymphatic flow of ultrafluid lipiodol from both lower extremities, the age of the patient;[1] previous therapy including steroids; and proliferation, replacement, or shrinkage of lymphoid tissue associated with disease, are important factors in determining the uptake of the oily contrast medium by lymph nodes. Increasing experience of the use of ultrafluid lipiodol for lymphography indicates that excessive deposition of this contrast medium in the lung is best avoided by careful fluoroscopic and roentgenographic monitoring during injection. It is generally agreed that optimal dosage is the minimum compatible with an adequate diagnostic lymphogram, and that serious complications using smaller amounts of oily contrast medium are extremely rare.

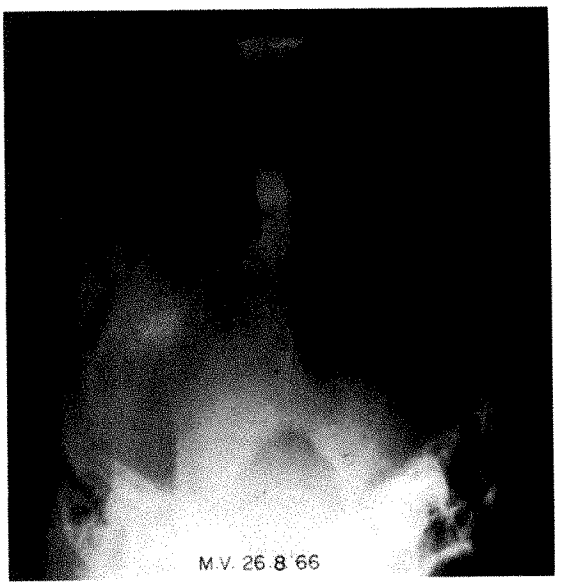


FIG. 3. Towne's projection of skull showing localized area of contrast material on the right side.

Although in the patient described, more account might have been taken of the recent weight loss, an average dose of ultrafluid lipiodol was introduced, and no roentgenographic evidence to suggest excessive deposition in the lung was demonstrated. The clinical diagnosis of cerebral complications following lymphography was confirmed by the demonstration of radiopaque material within the skull, and this was no longer present on repeat roentgenograms 12 hours later. In considering the normal efficacy of the lung as a filter for ultrafluid lipiodol, and the rarity of cerebral complications of lymphography performed as a premanagement procedure, the possibility that irradiation may have been a factor in producing systemic escape of the contrast medium in our patient was considered.

EXPERIMENTAL STUDY

Excessive introduction of ultrafluid lipiodol into the venous system either via the thoracic duct by using large doses of contrast medium for lymphography, or via lymphovenous communications, may result in visualization of small vessels, on the arterial side of the lung capillary bed.[7,16]

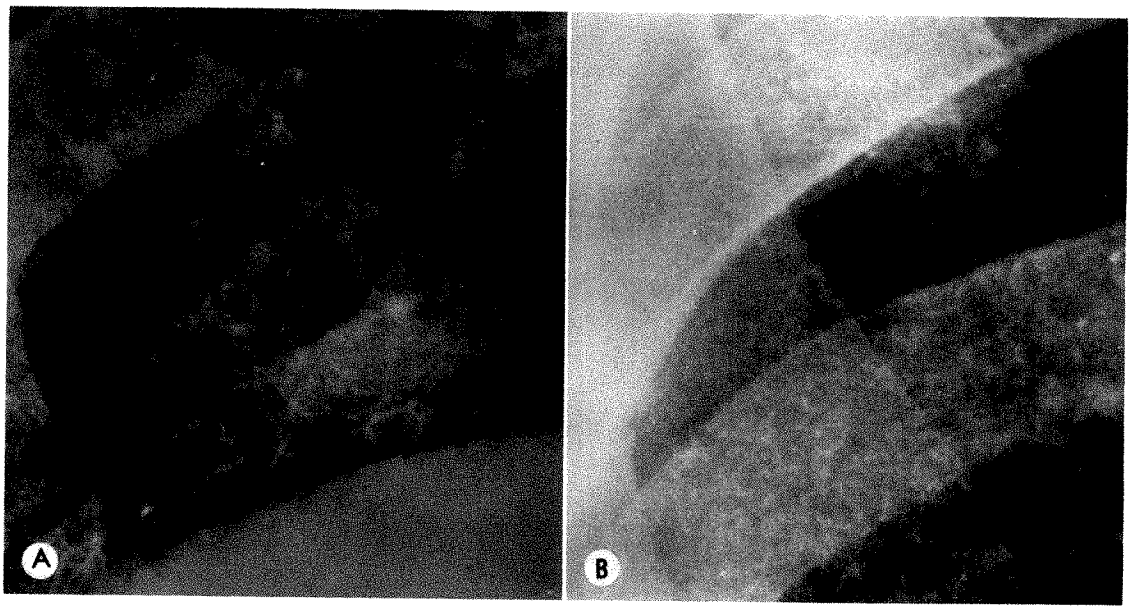


Fig. 4. Arborizing vascular patterns following lymphography. (*A*) Small vessels filled wtih contrast material. (*B*) At 24 hours, the same area shows a more diffuse stippled pattern.

Such arborizing microvascular* roentgenographic patterns seen in the lung (Fig. 4*A*) are more frequently recognized during or immediately following introduction of the contrast medium. At 24 hours, the commonly visualized granular stippling ensues (Fig. 4*B*), as the oily contrast material is transferred from the vascular lumen by the normal mechanisms.[5] Because external irradiation had been given prior to and immediately following lymphography in our patient, a preliminary study in rabbits was undertaken to investigate the influence of external irradiation on the disappearance time from the lung of the arborizing vascular pattern following intravenous injection of ultrafluid lipiodol.

METHOD

Twenty-five New Zealand white female rabbits weighing between 2 and 3 kg. were anesthetized by injection of nembutal (0.4 cc. per kg.) into the marginal vein of one ear. Through the same indwelling needle, 0.25 cc. of ultrafluid lipiodol, emulsified by hand in 1.75 cc. of distilled water, were introduced over a period of 5 minutes. To obtain more even distribution within the lungs, each rabbit was turned onto alternate sides several times during injection. While still anesthetized, anteroposterior and lateral roentgenograms of the chest were taken on each animal to visualize the appearances of contrast medium within the lungs.

Eight animals were re-roentgenographed prior to sacrifice at intervals of 1, 2, 4, 8, 16, 24, 48, and 72 hours following injection. Autopsy with histologic examination of the lung, brain, and kidneys was performed. A second group of 8 animals, following injection and initial roentgenography, were irradiated to 200 r with conventional 270 kev. radiotherapy (1.25 mm. Cu half-value layer; 50 cm. source-skin distance). A 5×8 cm. field covering the mediastinum, left lung, and middle third of the right lung field was used in each animal. A third group of 8 animals were similarly irradiated to 1,000 r. Following radiotherapy, roentgenography of the chest, sacrifice, and autopsy were performed at similar times to the unirradiated animals.

* Micro= of small size. Oxford English Dictionary.

ROENTGENOGRAPHIC FINDINGS

Arborizing patterns of ultrafluid lipiodol within the lungs were demonstrated in all of the rabbits following injection (Fig. 5). Irregular distribution of small contrast filled vessels was noted, and these were best identified at the periphery and bases of the lung fields. The lateral roentgenogram was particularly useful in gauging the extent of vessel opacification in the paramediastinal and posterior basal areas (Fig. 6).

Comparison of pre-irradiation and post-irradiation roentgenograms allowed identification of the presence or absence of the microvascular pattern, and a visual estimation of its extent. In addition, spot roentgenograms of areas of interest (Fig. 7, *A* and *B*) were used to increase the accuracy of appraisal of vascular patterns which were easily obscured by blurring due to rapid respiratory movement. An additional difficulty was the development of numerous confluent shadows within the lung similar to those described by Baert who found these appearances associated with pulmonary hemorrhages or hemorrhagic infarcts with small areas of atelectasis. In such areas, recognition of the arborizing pattern was difficult or impossible. These disadvantages may have been accentuated in this pilot experiment due to irregular introduction of the contrast medium by the crude emulsification method used.

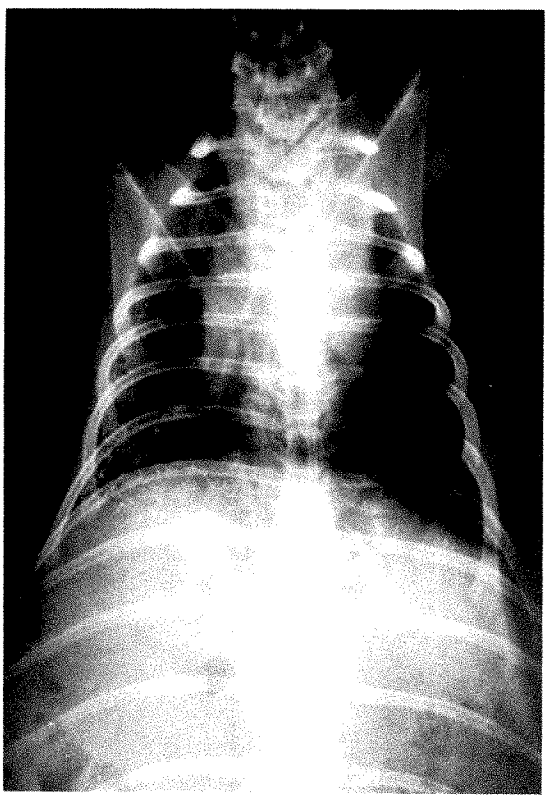


Fig. 5. Anteroposterior roentgenogram of rabbit showing the arborizing vascular pattern most marked in the lung bases and periphery.

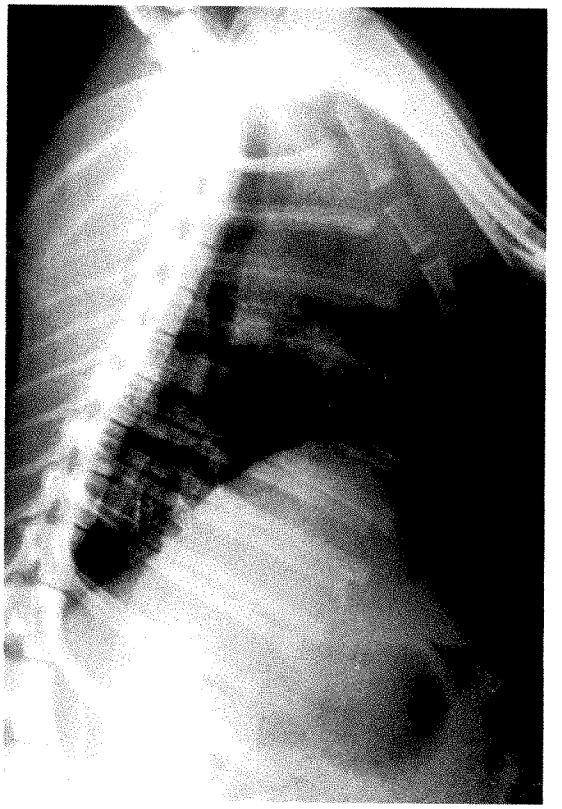


Fig. 6. Lateral roentgenogram showing arborizing vascular pattern projected over the cardiac shadow and in lung bases.

Each set of roentgenograms was submitted in a randomized fashion to 2 radiologists who independently recorded the presence or absence of the microvascular pattern. The extent of the arborizing pattern was graded on whether this was easily recognized and diffuse throughout the lung, or minimal but definite. Close agreement was found between the interpretations of

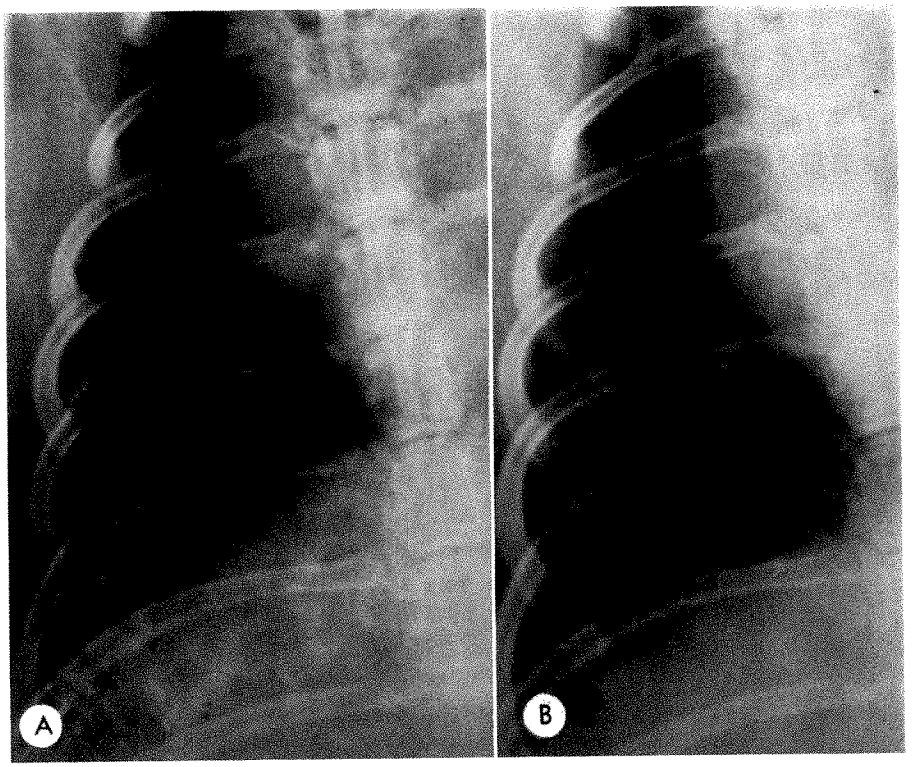


Fig. 7. (*A*) Spot roentgenogram showing arborizing vascular pattern. (*B*) Same projection showing loss of visualization due to respiratory movement.

each observer. In the unirradiated animals, a decrease in the extent of the arborizing pattern was noted as the time interval between injection and roentgenography increased to 24 hours. No evidence of vessel opacification was detected after this time. In none of the irradiated animals was an arborizing pattern recognized after a time interval of 16 hours from injection. A more rapid loss of the arborizing contrast pattern was observed in irradiated animals, and this was most marked in the 1,000 r group (Fig. 8).

The roentgenographic observations suggest that external irradiation may increase the rate of disappearance of the arborizing vascular pattern caused by intravenous injection of ultrafluid lipiodol in the rabbit lung. Limitations of the method and the small number of animals used in this pilot experiment preclude a definite conclusion. In no animal was contrast material recognized roentgenologically within the cranium or abdomen.

PATHOLOGIC FINDINGS

At autopsy, subpleural and intrapulmonary hemorrhages were found in all animals. Hematoxylin and eosin, and oil Red O stained sections of brain, lung, and kidney were examined. Ultrafluid lipiodol was present within the lumina of small pulmonary arteries and capillaries in all animals (Fig. 9). Eosinophilic infiltrations most marked in the septal walls with occasional multinuclear giant cells were noted, and small lipid droplets within macrophages could be seen. No significant differences could be identified between unirradiated and irradiated animals in the distribution of lipid within the vessels, septal walls, and alveoli. The macrophage and lymphocyte content of the lungs was similar in all animals, and lipid was identified within the capillaries in both irradiated and unirradiated animals at 72 hours.

Within the kidneys, vacuoles of lipid were easily identified in the glomeruli of several of the irradiated animals (Fig. 10).

In the 1,000 r group, increase in lipid content was observed at 2 hours, with numerous vacuoles in the glomeruli and within the cells of the proximal and distal convoluted tubules. A cellular reaction to lipid droplets was observed in those irradiated animals killed after 36 hours. In the more lightly irradiated group, increase in lipid content of the kidneys was also noted in comparison with unirradiated animals.

Examination of brain sections showed small areas of petechiae and foci of acute necrosis with surrounding cellular reaction. Only one such finding was observed in an unirradiated animal sacrificed 48 hours after injection, but 7 of the irradiated rabbits showed these changes at intervals of 2 to 48 hours. The most marked reaction in the brain was in the heavily irradiated rabbits sacrificed 16 hours after injection of the ultrafluid lipiodol.

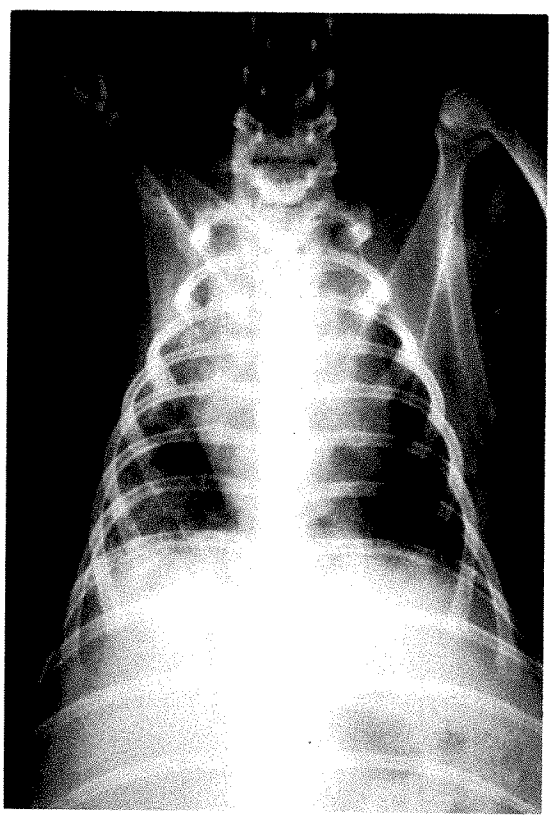


FIG. 8. Same animal as in Figure 5 two hours after 1,000 rads showing decrease in arborizing pattern.



FIG. 9. Lung section—arterioles showing intraluminal lipid with obliterative endarteritis. Lipid vacuoles are present in the adventitia, and a surrounding mononuclear cellular reaction is seen.

The above findings in both kidney and brain are consistent with an increase in escape of ultrafluid lipiodol into the systemic circulation in irradiated animals.

DISCUSSION

The complex mechanisms of vessel dilatation and increased permeability due to histamine and other agents following acute irradiation, have been extensively investigated.[8,10,13,20] An increase in vascular volume occurring shortly after an acute local dose of irradiation has been demonstrated in the rabbit ear, in addition to later changes in capillary permeability.[11] Although it has been observed that one of the earliest and most consistent reactions to roentgen irradiation of the chest is a change in the pulmonary vessels,[19] most studies on lung in this respect, have concentrated



Fig. 10. Glomerulus containing lipid vacuoles.

on radiation pneumonitis occurring at longer intervals after the episode or course of irradiation.[2,3,17] The induction of an arborizing vascular pattern which may be easily recognized on roentgenograms by intravenous injection of ultrafluid lipiodol may prove a further useful experimental method to enable assessment of the immediate effects of physical and chemical agents on vascular structures within the lung. The present study suggests that external irradiation decreases the filtration effect of the lung capillary bed for ultrafluid lipiodol in the rabbit.

In the patient described, the significance of performance of lymphography during whole chest irradiation in the production of cerebral lipid embolization due to ultrafluid lipiodol is unknown, and this specific relationship has not been recorded in other such episodes. It is felt that until further evidence is forthcoming, lymphography should not be performed during chest irradiation, and that its optimal place in investigation as a premanagement procedure should be maintained.

SUMMARY

1. The clinical, laboratory, and roentgenographic findings in a patient with cerebral complications following lymphography performed after commencement of radiotherapy to the chest are described.

2. A preliminary experiment to examine the possibility that external irradiation may influence the filtration mechanism, in the lungs of rabbits, for ultrafluid lipiodol injected intravenously, is recorded.

Department of Diagnostic Radiology
The Ontario Cancer Institute
500 Sherbourne Street
Toronto 5, Ontario, Canada

The assistance of Drs. Officer and Walker of the Department of Radiodiagnosis, Princess Margaret Hospital, Toronto, and Drs. Brown, Platts, and Partriquin of the Department of Pathology, is gratefully acknowledged. Irradiation for this experimental study was performed by Dr. R. D. T. Jenkin, Department of Radiotherapy. Animal facilities were kindly provided by Dr. Siminovitch and Mr. McKinley. The illustrations were prepared by the Department of Photography under the direction of Mrs. Gaettens. This manuscript was typed by Miss Ruth MacLean.

REFERENCES

1. Denz, F. A. Age changes in lymph nodes. *J. Path. & Bact.*, 1947, *59*, 575–591.
2. Ellinger, F. E. Medical Radiation Biology.
3. Englestad, R. B. Über die Wirkung der Röntgenstrahlen auf die Lungen. *Acta radiol.*, 1935, Suppl. 19.
4. Fischer, H. W. Reviewer's comments. *Invest. Radiol.*, 1967, *2*, 319.
5. Fraimow, W., Wallace, S., Lewis, P., Greening, R. R., and Cathcart, R. T. Changes in pulmonary function due to lymphangiography. *Radiology*, 1965, *85*, 231–241.
6. Hallgrimsson, J., and Clouse, M. E. Pulmonary oil emboli after lymphangiography. *A.M.A. Arch. Path.*, 1965, *80*, 426–430.

7. Ishida, O., Yoshihiro, T., Mori, S., and Uchida, H. Chest radiograms following lymphography with special reference to oil embolism. *M. J. Osaka Univ.*, 1964, *14*, 275–303.
8. Jolles, B., and Harrison, R. G. Enzymic processes and vascular changes in skin radiation reaction. *Brit. J. Radiol.*, 1966, *39*, 12–18.
9. Koehler, P. R., Meyers, W. A., Shelley, J. F., and Schaffer, B. Body distribution of ethiodol following lymphangiography. *Radiology*, 1964, *82*, 866–871.
10. Mount, D. W. A. Quantitive studies of vascular effects of x-irradiation. Master of Arts Thesis, University of Toronto, 1962.
11. Mount, D., and Bruce, W. R. Local plasma volume and vascular permeability of rabbit skin after irradiation. *Radiation Res.*, 1964, *23*, 430–435.
12. Nelson, B., Rush, E. A., Takasugi, M., and Wittenberg, J. Lipid embolism to brain after lymphography. *New England J. Med.*, 1965, *273*, 1132–1134.
13. Rigdon, R. H., and Curl, H. Effect of roentgen irradiation on capillary permeability and inflammation in skin of rabbit. Am. J. Roentgenol. & Rad. Therapy, 1943, *49*, 250–257.
14. Ruttiman, A. Editor. Proceeds in Lymphology: Proceedings of the First International Symposium on Lymphology, Zürich, Switzerland, July 19–23, 1966. Georg Thieme Verlag, Stuttgart, Germany.
15. Schaffer, B., Koehler, P. R., Daniel, C. R., Wohl, G. T., Rivera, E., Meyers, W. A., and Shelley, J. F. Critical evaluation of lymphangiography. *Radiology*, 1963, *80*, 917–930.
16. Takahashi, M., and Abrams, H. L. Arborizing pulmonary embolization following lymphangiography: report of three cases and experimental study. *Radiology*, 1967, *89*, 633–638.
17. Teates, D., and Cooper, G., Jr. Some consequences of pulmonary irradiation: second long term report. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1966, *96*, 612–619.
18. Threefoot, S. A. Pulmonary hazards of lymphography. *Cancer Chemother. Rep.*, 1968, *52*, 107–111.
19. Tobin, C. E. Experimental pulmonary thromboemboli in rats after thoracic x-irradiation. *Radiation Res.*, 1965, *24*, 538–546.
20. Willoughby, D. A. Pharmacological aspects of vascular permeability changes in rat's intestine following abdominal radiation. *Brit. J. Radiol.*, 1960, *33*, 515–519.

CONTRAST-VASOCONSTRICTOR MIXTURES IN ANGIOGRAPHY*

By PAUL C. KAHN, M.D.
With the Technical Assistance of Joseph P. Zeppieri, A.B.,† *and* Gerald S. Lorch, B.S.†
BOSTON, MASSACHUSETTS

THE value of the vasoconstrictor effect of epinephrine in angiography has now been well documented.[1,3,6,7,8] In most techniques the vasoconstrictor and the contrast medium are introduced sequentially with a variable time interval between the 2 injections. After intra-arterial administration the vascular response is almost instantaneous in onset, but also fades rather quickly. For this reason it was considered that the administration of a mixture of contrast media and catecholamines might prove an ideal method of standardizing and simplifying epinephrine angiographic techniques, as well as minimizing the dose of vasoconstrictor. A series of experiments in dogs partly substantiated this assumption, but also resulted in some interesting, but unexpected observations. The results of these experiments, as well as the preliminary clinical application of these mixtures are presented.

MATERIAL AND METHODS

Twenty-two experiments were performed on 9 mongrel dogs weighing 33 to 40 pounds. They were anesthetized with sodium pentobarbital, 0.2 mg. per pound. A cut-down was performed on a femoral artery and a PE 240 (Clay-Adams) polyethylene catheter was inserted into the abdominal aorta and positioned at the T 12—L 1 level. The electrocardiogram and the brachial arterial pressure were recorded on a Sanborn 964 recorder. Serial aortograms were obtained on a Sanchez-Perez film changer following the injection of 1 ml. per pound of each of the following: (1) Methylglucamine iothalamate 60 per cent (contrast); (2) methylglucamine iothalamate with 1 microgram of epinephrine per ml.; (3) methylglucamine iothalamate with 5 micrograms of epinephrine per ml.; and (4) methylglucamine iothalamate with 1 microgram l-norepinephrine (levophed) per ml. The injections were randomized and not identified until after the data interpretation had been completed. There was at least a 45 minute delay between successive aortographies. Two injection speeds were used, one delivering the bolus in 1.5 seconds, the other in 7.5 seconds. The same speed was used throughout each experiment. Twelve roentgenograms spaced over a period of 21 seconds were taken with each injection. Each dog was studied up to 4 times, with a rest interval of at least 3 days. Hemoglobin and serum creatinine were measured regularly. An autopsy was performed after the last experiment.

RESULTS

The hypotensive phase lasting 1 to 2 minutes after the injection of contrast media is well known[4] and was clearly demonstrated in our animals, with a mean blood pressure drop of 25 mm. Hg (Fig. 1). The addition of 1 μg. per ml. of epinephrine reversed the curve, with a rise in blood pressure of about 25 mm. now measured. The addition of 5 μg. of epinephrine per ml. resulted in a much more marked blood pressure rise. The 1 μg. per ml. dose of l-norepinephrine was intermediate between these two, corresponding roughly to 2 μg. per ml. of epinephrine. Changes in heart rate were also apparent. Epinephrine prolonged the tachycardia which followed the

* Presented at the Sixteenth Annual Meeting of the Association of University Radiologists, Columbus, Ohio, May 8–11, 1968.
From the Department of Radiology, New England Medical Center Hospitals, Boston, Massachusetts.
Supported by USPHS Research Grant No. HE 09624.
† Summer Fellows, Department of Radiology, Tufts University School of Medicine.

injection of the contrast agent alone, but levophed diminished this effect, and, in fact, produced a slight bradycardia after 2 to 3 minutes.

The effects of these mixtures on the aortogram were quite striking (Fig. 2, *A* and *B*). The aortic blood flow was markedly reduced, and the slow injections of contrast-vasoconstrictor mixtures resulted in a complete aortogram, while in the control injections only faint aortic visualization was present. The renal arteries were filled out, although peripheral constriction could be seen. Adrenal visualization was usually improved in the injections with vasoconstrictors; however, the improvement was not really pronounced except when the large dose of epinephrine was employed (Fig. 3, *A* and *B*). Slightly increased opacification of the lumbar artery branches was also noted.

One of the most surprising results was the prolonged, dense nephrogram seen after the injection with vasoconstrictors. Excellent parenchymal visualization was obtained 20 seconds after the injection, long after it had faded in the controls (Fig. 4, *A* and *B*). Epinephrine and levophed appeared comparable in this effect, which was only slightly related to dose (Fig. 5). Along with persistent increase in density, a decrease of renal size of 2 to 3 mm. was found.

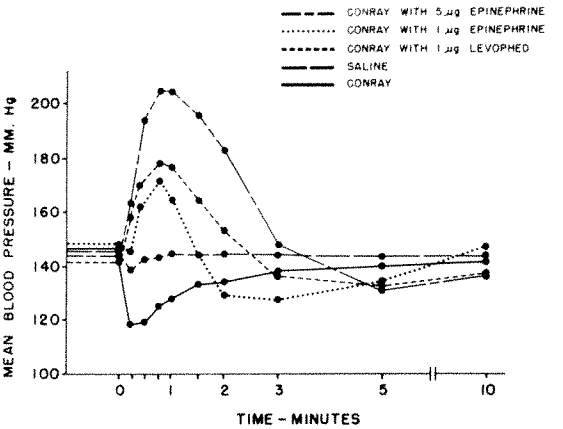


Fig. 1. Effect of contrast-vasoconstrictor mixtures on blood pressure. Abdominal aortogram with 1 ml. per pound of each mixture in dogs. Note that the contrast-vasoconstrictor combinations reverse the normal hypotensive phase seen with the control injection.

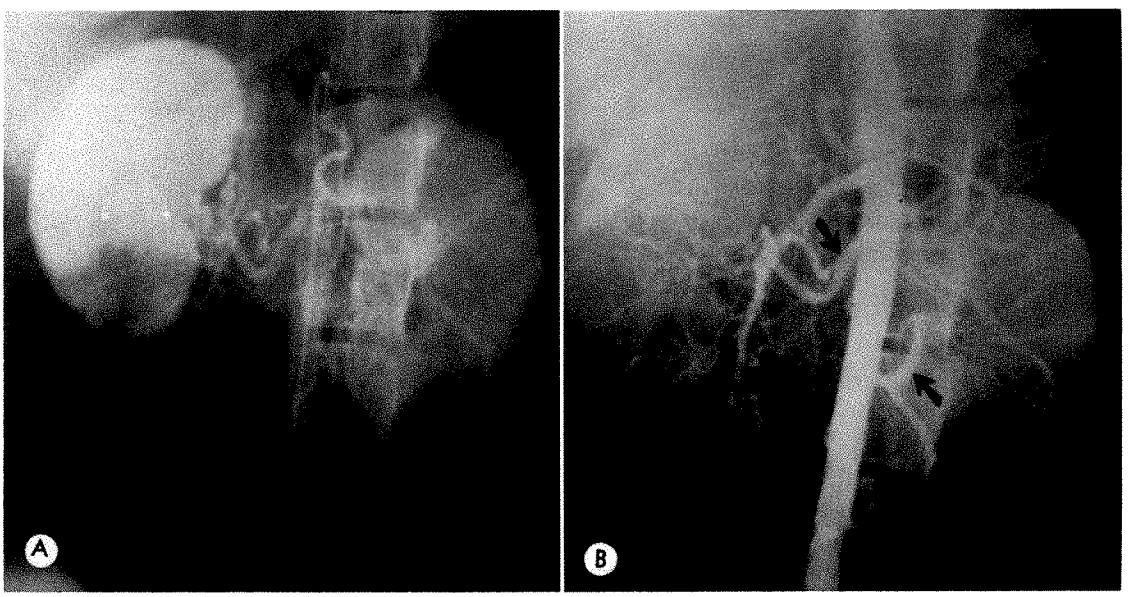


Fig. 2. (*A*) Aortogram at the conclusion of a 7.5 second injection of 38 ml. of conray 60 in a 38 pound dog. Note that very little contrast material remains in the aorta and major arteries. (*B*) Repeat aortogram with 1 μg. per ml. of epinephrine added to the contrast material. Roentgenogram at the end of injection shows dense filling of the aorta and most branches. The renal arteries (arrows) are well filled proximally, but are constricted peripherally.

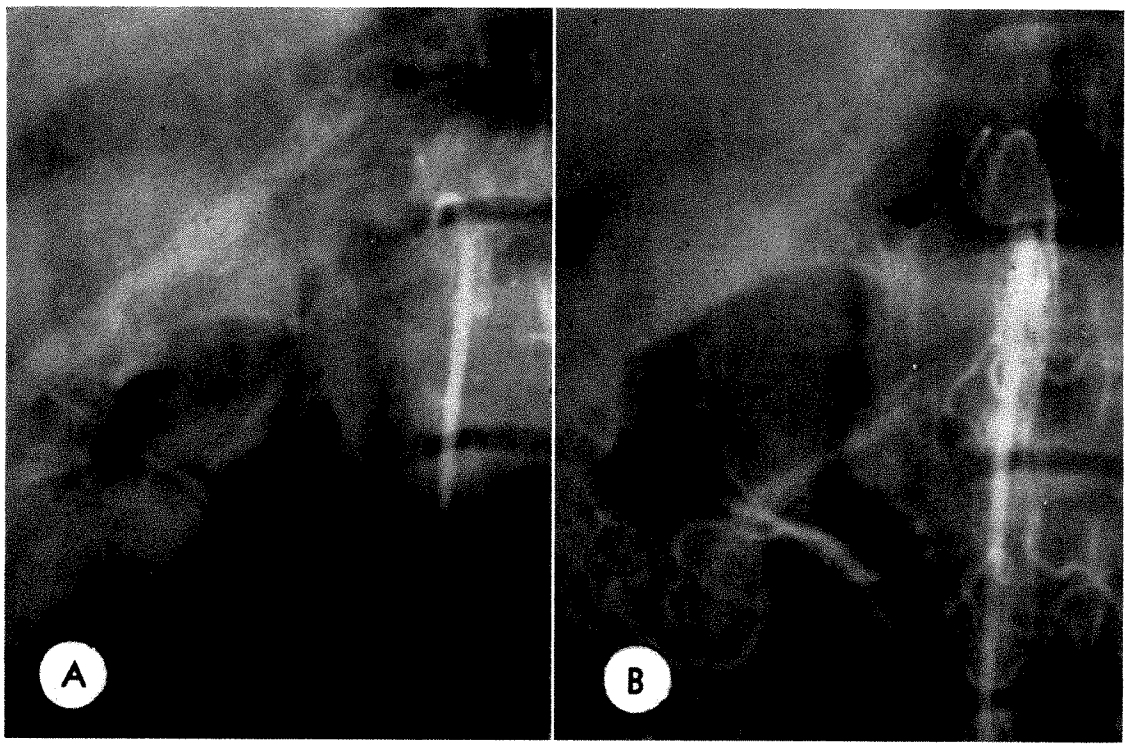


Fig. 3. (*A*) Conray aortogram shows a density medial to the right kidney faintly suggesting an adrenal gland. (*B*) Repeat aortogram with 5 μg. per ml. epinephrine added to the contrast agent shows a dense adrenal arteriogram (arrows). Roentgenograms with 1 μg. per ml. of epinephrine or l-norepinephrine were only slightly better than the control.

DISCUSSION

Slowing of aortic blood flow with contrast-vasoconstrictor mixtures is expected. While the renal and gastrointestinal circulations are most reduced, flow through the muscular branches also decreases slightly. The ability to produce a satisfactory aortogram with a prolonged injection is potentially clinically useful. For example, good roentgenograms could be obtained through a small translumbar needle. With a catheter aortogram, a manual rather than a pump injection could be used.

Another potential application might be for adrenal visualization.[9] However, the large dose of epinephrine required to obtain good adrenal filling is not practical for clinical use at present. A combined pharmacologic approach with vasoconstrictors plus other stimulants of adrenal blood flow (*e.g.*, angiotensin or ACTH) may prove more rewarding.

The prolonged nephrogram after injection of the contrast-vasoconstrictor mixtures requires some explanation. When epinephrine and a contrast agent are administered sequentially, practically no nephrogram is obtained.[5] This is due to the marked vasoconstriction of the renal arteries. One must assume that when the mixture is used some of the contrast material enters the small renal vessels before vasoconstriction occurs, and then is trapped by the cessation of blood flow. Although there is potential clinical application for this prolonged nephrogram, for example in nephrotomography, this technique must be approached with caution. It is generally believed that one of the parameters of renal toxicity of contrast medium is the length of time which the contrast material remains within the renal parenchyma.[2] However, none of the animals in this study developed serum creatinine elevations, despite repeated injections with

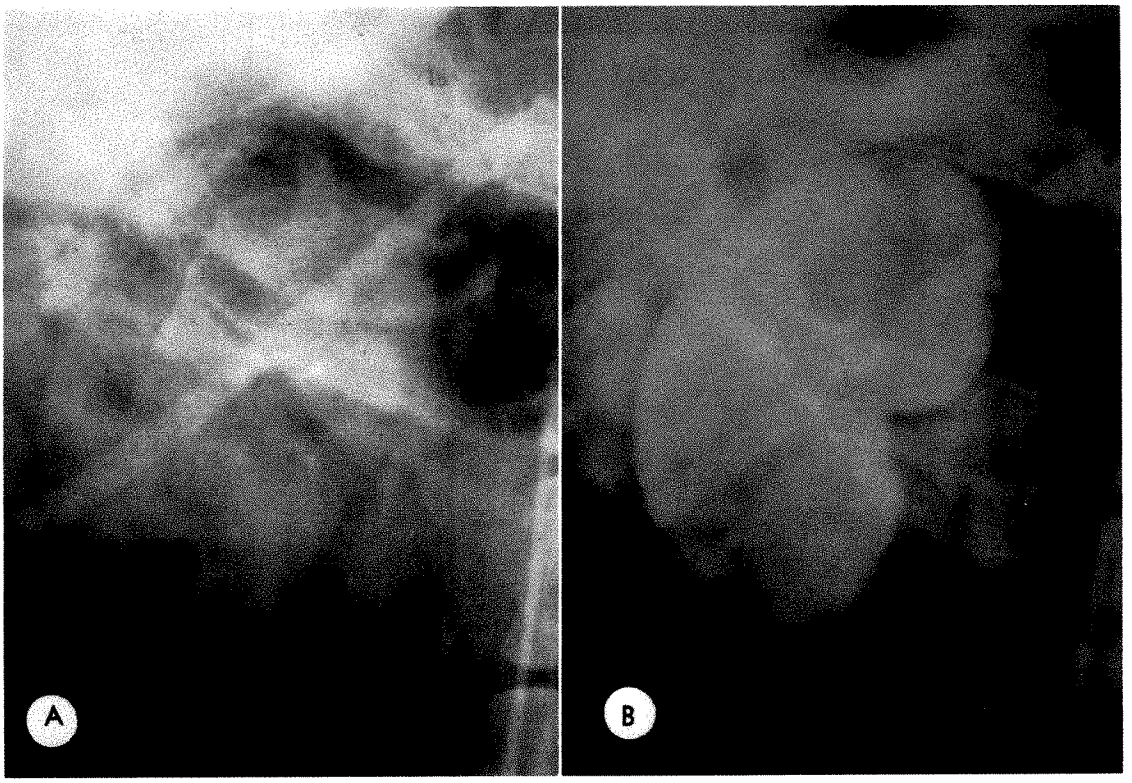


FIG. 4. (*A*) Conray aortogram 15 seconds after injection shows only a faint residual nephrogram. (*B*) Aortogram 15 seconds after an injection with a mixture of 1 μg. per ml. of epinephrine in the contrast material shows a dense nephrogram. The kidney is reduced 3 mm. in length.

doses 2 to 3 times as great on a weight basis as would be used in patients.

The elimination of the hypotensive phase of the contrast medium injection by the use of vasoconstrictors offers another possibility for clinical application. It has been assumed that some of the serious sequelae of contrast injections may be due to this hypotension. Only a very small amount of epinephrine is required to eliminate this effect. Because this dose is well within the range used for tumor evaluation (*e.g.*, 10–15 μg.) a limited clinical trial was made. In a few patients, mixtures of 0.2 μg. of epinephrine per ml. of methylglucamine iothalamate 60 per cent (conray) were used for distal aortic injection well below the renal arteries during femoral arteriography. Twenty to thirty milliliters of the mixture was used for one of 3 to 4 injections usually done as part of the procedure, and blood pressure was monitored through the catheter after all of the injections. The addition of epinephrine largely eliminated the 10–15 mm. blood pressure drop present in other injections. No difference was seen in the filling of the muscular branches of the lower extremity arteries. Interestingly enough, the patients noted markedly less discomfort with the injection of the contrast-epinephrine mixture.

CONCLUSION AND SUMMARY

An experiment was designed to test in dogs the effectiveness of mixtures of epinephrine and l-norepinephrine with methylglucamine iothalamate (conray) as a method of utilizing the epinephrine effect in arteriography.

It was shown that the use of such combinations can reverse the hypotensive phase which ordinarily occurs after contrast medium injections.

A reduction of aortic blood flow, which is

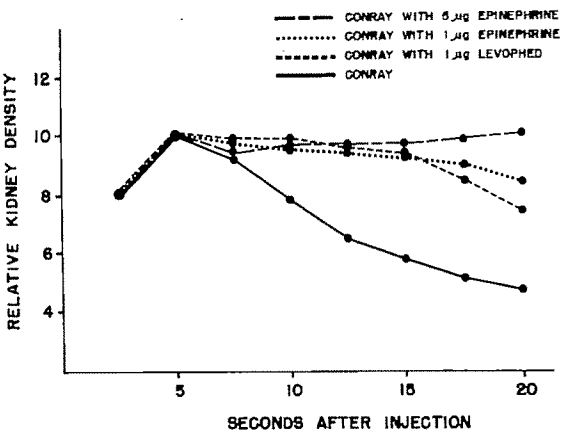


FIG. 5. Effect of addition of vasoconstrictors on the persistence of the nephrogram after arteriography. Note that the nephrogram fades rapidly after the control injection. With the contrast-vasoconstrictor mixtures the nephrogram remains intense for 15 to 20 seconds.

potentially useful in angiography, was noted.

A dense persistent nephrogram seen after the injection of the contrast-vasoconstrictor mixtures was attributed to trapping of contrast medium in the kidneys.

Improved adrenal visualization could also be obtained, but only when larger doses of epinephrine were used than are clinically practical.

Paul C. Kahn, M.D.
Department of Radiology
New England Medical Center Hospitals
171 Harrison Avenue
Boston, Massachusetts 02111

REFERENCES

1. ABRAMS, H. L. Response of neoplastic renal vessels to epinephrine in man. *Radiology*, 1964, *82*, 217–224.
2. BODFORSS, B., MUTH, T., and OLIN, T. Renal function judged with radioactive diodrast after selective renal angiography in dogs. *Acta radiol.* (Diag.), 1964, *2*, 449–459.
3. BOIJSEN, E., and REDMAN, H. Effect of epinephrine on celiac and superior mesenteric angiography. *Invest. Radiol.*, 1967, *2*, 184–199.
4. EFSEN, F., and MUNKNER, T. Influence of abdominal aortography on arterial blood pressure, cardiac output and heart rate. *Invest. Radiol.*, 1968, *3*, 6–14.
5. KAHN, P. C. Epinephrine effect in selective renal angiography. *Radiology*, 1965, *85*, 301–305.
6. KAHN, P. C., FRATES, W. J., and PAUL, R. E., JR. Epinephrine effect in angiography of gastrointestinal tract tumors. *Radiology*, 1967, *88*, 686–690.
7. KAHN, P. C., and WISE, H. M., JR. Use of epinephrine in selective angiography of renal masses. *J. Urol.*, 1968, *99*, 133–138.
8. ROCKOFF, S. D., DOPPMAN, J., BLOCK, J. B., and KETCHAM, A. Variable response of tumor vessels to intra-arterial epinephrine: angiographic study in man. *Invest. Radiol.*, 1966, *1*, 205–213.
9. WINKLER, S. S., and KAHN, P. C. Pharmacologic aids in adrenal angiography. *Invest. Radiol.*, 1967, *2*, 48–52.

VOL. 105, NO. 4

EFFECT OF ANGIOCARDIOGRAPHY ON FLUID AND ELECTROLYTE BALANCE*

By AARON R. LEVIN, M.R.C.P. (EDIN.), HERMAN GROSSMAN, M.D., EDWARD T. SCHUBERT, PH.D., PATRICIA WINCHESTER, M.D., *and* ANGELA GILLADOGA, M.D.
NEW YORK, NEW YORK

DESPITE the wide use of contrast media during cardiac catheterization and visual contrast studies, there have been few reports concerned with the changes in fluid and electrolyte balance associated with the diagnostic use of these substances. A number of investigators have demonstrated that there is a rise in the serum osmolality after the use of contrast medium and have indicated the associated danger if such changes are marked and unheeded.[1–4] Others have concentrated their observations on the causes and effects of the acidosis following angiocardiography.[5,6,7] However, a review of the available literature has failed to reveal any comprehensive study involving the effects of contrast media on all the electrolytes and on fluid balance. It is the purpose of this investigation, therefore, to determine the acute effects of angiocar liography on fluid and electrolyte balance in infants and children with congenital heart disease.

MATERIAL AND METHODS

The material consisted of 33 patients between the ages of 1 month and 18 years who underwent diagnostic cardiac catheterization and angiocardiography. Thirteen patients were under 1 year of age and 14 were cyanotic. Twenty patients had 2 angiocardiographies, making a total of 53 individual studies. Hypaque-M 75 per cent (sodium and meglumine diatrizoates) was injected with a Gidlund injector which was programmed to deliver the bolus of 1 ml./kg. body weight in 1 second through either NIH or Kifa catheters. Control values for concentrations of serum sodium, chloride, potassium, bicarbonate, and osmolality, and for the blood urea nitrogen, pH, hemoglobin and hematocrit were obtained just prior to the injection of contrast media. Following the injections, samples were drawn within 5 minutes, and then at 15, 30 and 180 minutes thereafter. Blood for pH was sampled from the systemic arterial circulation, and was measured with an Instrumentation Laboratories pH meter. Serum sodium and potassium were measured by an Instrumentation Laboratories flame photometer. Chlorides were determined with a Cotlove chloridometer by the amperometric technique. Serum osmolality was obtained by the method of freezing point depression utilizing an Advance Instruments osmometer. The Berthelot reaction was used to determine the blood urea nitrogen, and the Natelson's Gasometer employed for the bicarbonate estimations. The hematocrit and hemoglobin analyses were performed by standard laboratory techniques. Ultramicro methods were employed throughout, and each time-determination for all parameters required 1.5 cc. of blood.

In the majority of instances, blood samples were obtained through the same catheter which was utilized for the angiocardiography. Following the injection, however, the residual contrast medium was removed and the catheter repeatedly flushed with 5 per cent dextrose water. The first blood sample on withdrawal was discarded. To rule out the possibility of residual contrast material in the catheter affecting the results, in 5 patients blood samples were obtained for analyses from a second catheter which had not been utilized during the angiocardiographic procedure. The results in these latter in-

* Presented at the Sixteenth Annual Meeting of the Association of University Radiologists, Columbus, Ohio, May 8–11, 1968.
From the Departments of Radiology and Pediatrics, New York Hospital—Cornell University Medical Center, New York, New York.

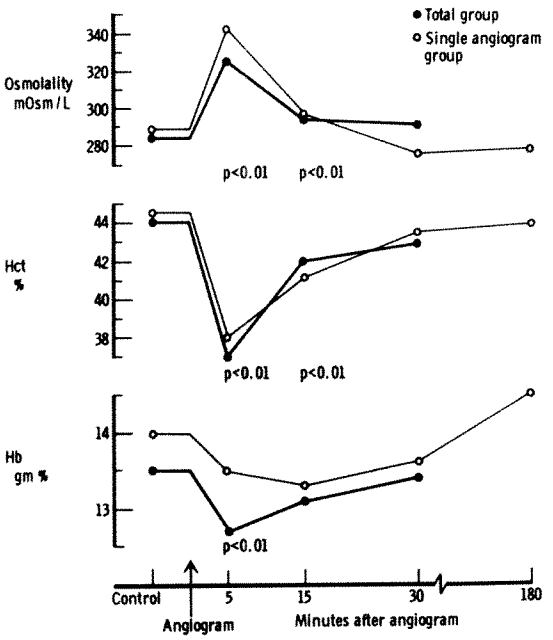


FIG. 1. Serum osmolality, hemoglobin and hematocrit. Mean values for 2 groups of patients: open circles are those patients having a single angiocardiography and the solid circles represent the total group of patients studied, those having a single and second angiocardiography.

stances revealed the same changes in all parameters measured as was obtained in all other patients.

RESULTS

The major change in the electrolyte and fluid balance was obtained within the first 5 minutes after the first angiocardiogram. The changes were consistent for the osmolality, hemoglobin and the hematocrit and for the various electrolytes, except for the sodium and chloride estimations. Figure 1 illustrates the changes obtained in 2 groups of patients for the serum osmolality, hemoglobin and hematocrit. One group of 20 patients had a second angiocardiography and their values for these parameters are plotted for only 30 minutes, whereas the remaining group of patients had only 1 angiocardiography and the determinations are plotted to 180 minutes. For each parameter, the same pattern of change occurred in each group of patients.

The serum osmolality showed a mean rise from a control value of between 285 and 290 mOsm/L to figures well above 320 mOsm/L within the first 5 minutes, a rise of between 10 and 12 per cent. By 15 minutes after the angiocardiography, the osmolality had almost reached the normal range, and thereafter was at or even below normal. Both the hematocrit and the hemoglobin showed a dramatic fall at 5 minutes of 14 to 18 per cent. A return toward normal values was seen at 15 minutes and was almost complete at 30 minutes. The changes in osmolality, hematocrit and hemoglobin were statistically significant, with p values of less than 0.01.

The changes observed in serum sodium and in serum chloride (Fig. 2) were not statistically significant. Although the mean values shown suggest an upward trend in the serum sodium within the first 5 minutes after angiocardiography, a review of the data obtained in the total group of pa-

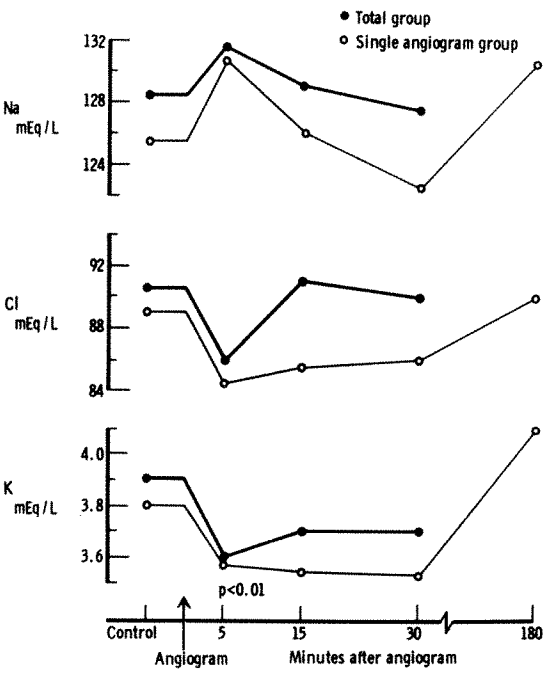


FIG. 2. Serum sodium, chloride and potassium. Although sodium and chloride demonstrate a change, the differences were not statistically significant. The fall in the potassium was significant at a p value of less than 0.01.

tients revealed no consistent pattern in the response of the sodium to the introduction of contrast medium. The slight fall in serum chloride was also insignificant and also showed no consistent pattern of change for the entire group of patients. However, the serum potassium fell sharply within 5 minutes of injection and showed a more gradual return towards the control values. The changes for potassium (Fig. 2) were significant at a p value of less than 0.01.

The changes in serum carbon dioxide content, blood urea nitrogen and pH are depicted in Figure 3. All parameters have the same tendency to fall sharply within 5 minutes of injection, each mean value being lower than the control, and the difference was statistically significant at this time, with a p value of less than 0.01. Fifteen minutes following the injection of contrast medium there was a rebound towards control values, most marked in the pH readings which showed complete recovery.

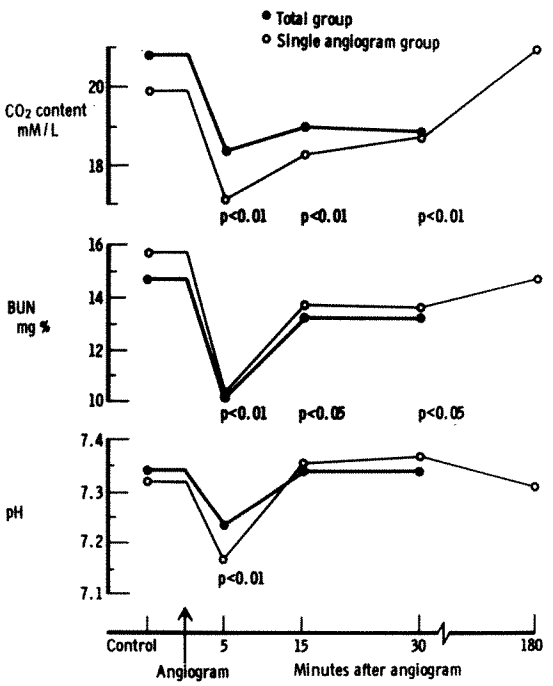


Fig. 3. Serum carbon dioxide content, blood urea nitrogen, and pH. There was a statistically significant fall in all these parameters within 5 minutes after the injection of contrast material, with a rapid rebound within 15 minutes.

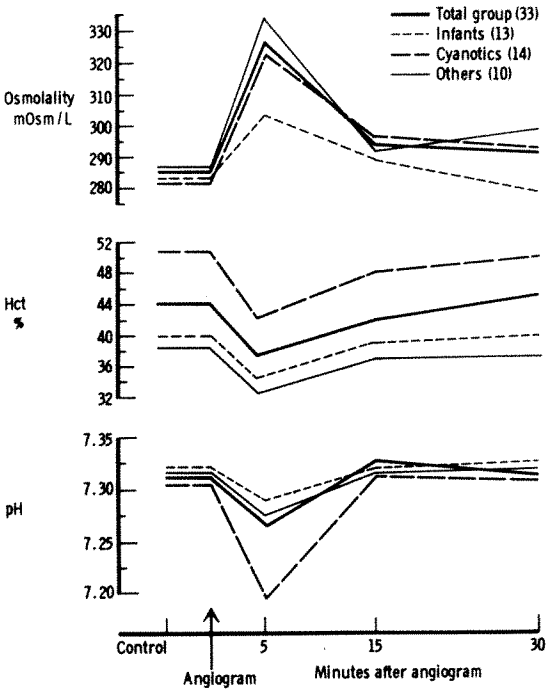


Fig. 4. Serum osmolality, hematocrit and pH for the subgroups studied showed the same pattern of response as the total group.

In comparing the changes in osmolality, hematocrit and pH for the entire group of patients with subgroups consisting of infants, cyanotic patients and the remaining patients, it was evident that all groups showed the same pattern of response (Fig. 4). However, in infants, the changes in osmolality showed less rise than in older patients. Similarly, the changes in pH for all the defined groups was similar, but cyanotic patients showed a greater fall in blood pH following angiocardiography within the first 5 minutes than did the other defined groups.

In 20 patients a second angiocardiography was performed 30 minutes after the first injection of contrast medium, and the final sample in this group was drawn 180 minutes after the second injection. The changes in the various parameters outlined above showed essentially the same pattern for both the first and the second angiocardiography (Fig. 5).

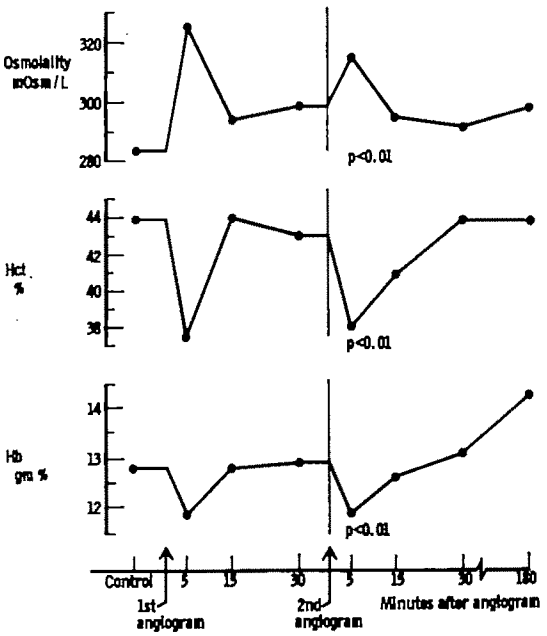


FIG. 5. Serum osmolality, hematocrit and hemoglobin of the 20 children undergoing a second angiocardiography show the same patterns as with the first when more than 30 minutes elapse between injections.

The serum osmolality rose from a mean figure of 284 mOsm/L to 326 mOsm/L following the first angiocardiography and showed a similar rise following the second angiocardiography, with a return towards normal values thereafter. The changes for hematocrit and hemoglobin (Fig. 5) also exhibited the same pattern of change after the second angiocardiography as occurred following the first. The values depicted in Figure 5 are statistically significant.

The serum sodium again showed no consistent pattern of change. Following the first angiocardiography, there was a rise in the mean values of serum sodium which tended to persist for the 30 minute interval before the second angiocardiography was performed. Following the second angiocardiography (Fig. 6), however, a marked fall in the serum sodium occurred with a fall to a level slightly lower than that of the control sample. This drop in value was statistically significant at the 0.05 level and the serum sodium subsequently rose during the remaining period of the study. Minor changes were noted in the serum chloride values with a definite fall following both the first and second angiocardiography. The same pattern of change was noted for the serum potassium.

In Figure 7, the carbon dioxide content, blood urea nitrogen and pH values show the same pattern of change for both the first and second angiocardiography as was noted in the group of patients who underwent one angiocardiography. The changes were significant and similar to those shown for the other parameters after both injections.

DISCUSSION

The replacement of inorganic water soluble iodine salts for contrast visualization studies by organic water soluble iodine compounds has greatly reduced the hazards

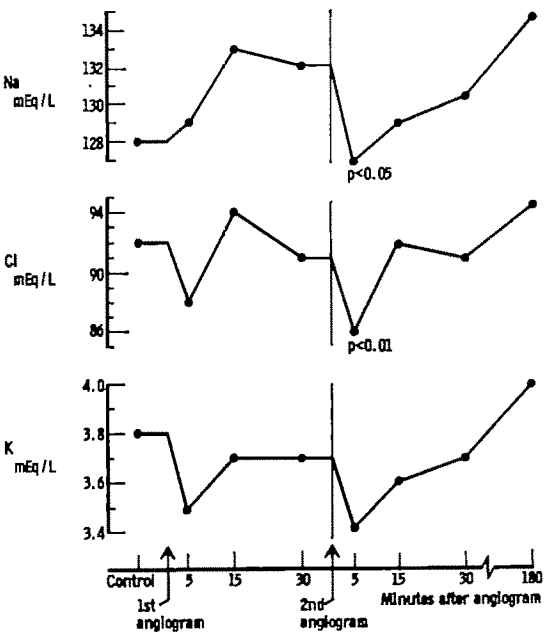


FIG. 6. With a second angiocardiography, 30 minutes after the first, the chloride and potassium show an initial drop in mEq/L within 5 minutes. The sodium concentration, after the first angiocardiography, became elevated from the baseline values and remained elevated until the second angiocardiography, when there was a drop during the first 5 minutes and then a steady rise through the study period of 180 minutes.

of angiocardiography. Hypaque M 75 per cent (sodium and meglumine diatrizoates) has an osmolality of 2,470 mOsm/L with a pH of between 6.5 and 7. Its introduction into the vascular system results in an increase in the serum osmolality. It has been shown by Giammona and co-workers[3] that serum osmolality in excess of 350 to 330 mOsm/L for any length of time may result in cerebral damage because of cellular dehydration. The mean values obtained in this study for the entire group of patients immediately after angiocardiography was 336 mOsm/L. The highest value recorded was 394 mOsm/L in a 5 year old boy with an atrial septal defect. These chemical changes in the blood are short-lived unless angiocardiography is repeated within a brief period.

The fall in other parameters at the same time as the recorded rise in serum osmolality would indicate a dilutional effect occurring within 5 minutes of injection. It is probable, therefore, that the osmolality being measured was not the peak reached,

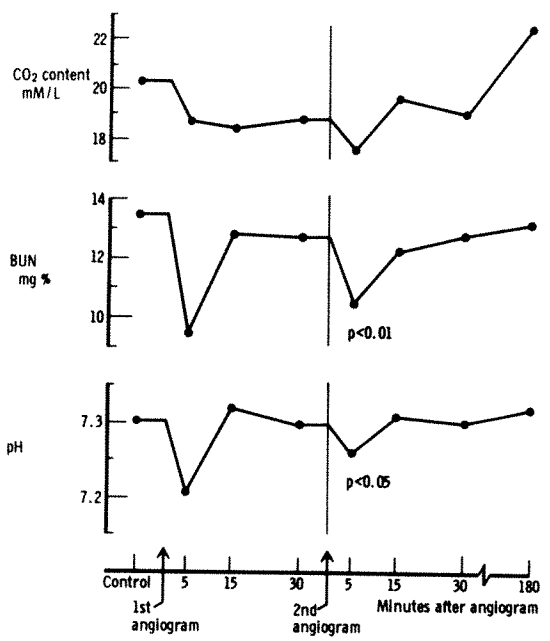


FIG. 7. The carbon dioxide content, blood urea nitrogen and pH have similar patterns after the first and second angiocardiography and these changes are significant.

but rather one that was already being affected by a dilutional process. As the peak osmolality is probably in excess of the figures shown, the repetition of an angiocardiography without allowing 20 to 30 minutes for recovery may be attended by real danger. Altman *et al.*[1] have shown that cerebral manifestations may occur more often in cyanotic babies. They further noted that in this group of patients lethargy and depression may occur for several hours after angiocardiography. For this reason, they have suggested the use of a Hypaque-M 50 per cent which has an osmolality of approximately 1,550 mOsm/L with an expected change in serum osmolality of a lesser magnitude than those reported in the present series and by other authors following angiocardiography.

The dilutional effect of Hypaque-M 75 per cent was documented by the fall in the other electrolyte parameters measured immediately after angiocardiography and particularly by the marked fall in the hematocrit. This probably results from the movement of water into the vascular compartment. With the excretion of contrast medium, the electrolyte balance is restored rapidly. Indeed, opacification of the bladder is seen within a few minutes after angiocardiography. We have not attempted to directly measure the changes in blood volume, but the marked fall in hematocrit of between 14 and 18 per cent would indicate that the increase in blood volume is significant. Kloster *et al.*[4] in their study of 80 adult patients also showed a fall in the hematocrit following angiocardiography. They considered this change to be due to the shrinkage of the red blood cells resulting from cellular dehydration following the introduction of a hyperosmolar solution into the blood stream, and to the transfer of fluid from the extracellular space to the intravascular compartment. These authors showed that an injection of 30 cc. of sodium iothalamate with an osmolality of 2,264 mOsm/L was capable of increasing the blood volume by approximately 230 cc. of fluid. It may be

estimated that in infants following an injection of 5 cc. of Hypaque-M 75 per cent, the increase in blood volume would be of the order of 30 to 35 cc. of fluid. The rapid increase in blood volume in patients with an already overloaded heart and in cardiac failure may further increase the hemodynamic burden.

Such an occurrence may explain the sudden demise that has been reported in such infants following angiocardiography. In the neonatal period also, the rapid increase in blood volume may be fraught with danger because of immature and suboptimal kidney function, especially if cardiac failure is superimposed

The marked fall in pH cannot be explained as a dilutional effect. In addition to the introduction of an acid substance being a possible cause, others have postulated a direct effect on the cell membrane with the release of hydrogen ions. Marshall and Henderson[5] have shown, following the use of Conray 280 in adult patients, that a tendency to acidosis was present. They further noted that the degree of acidosis that developed was directly related to the amount of contrast medium injected. The greatest fall in pH in the present series occurred in a 3 year old boy with transposition of the great arteries, ventricular septal defect and pulmonary stenosis, in whom the pH fell from 7.300 to 6.965 immediately after the second angiocardiography. This returned to normal within 15 minutes and the patient suffered no ill effects. However, in cyanotic ill patients with a tendency to acidosis, the insult of Hypaque-M may aggravate the situation and drop the pH further, leading to other difficulties such as depression of cardiac function and arrhythmia.

It seems evident, therefore, that the effects of contrast media on the fluid and electrolyte balance are profound, and repeated injections in cyanotic patients with congenital heart disease or in those with congestive heart failure may be fraught with danger if such injections are repeated in rapid succession without due regard being given to the quantity utilized. In a number of patients not included in the present series in whom a second angiocardiography was repeated within 15 minutes of the first and who received 1 ml./kg. body weight of Hypaque-M 75 per cent, the pattern of change following the second angiocardiography was even more pronounced than that following the first. We feel, therefore, that more than 20 minutes should be allowed to elapse between angiocardiographies, if repeated studies are indicated, to allow recovery from the acute biochemical insult produced by water soluble contrast material such as Hypaque-M on fluid electrolyte balance.

SUMMARY

A study of the effects of contrast material on fluid and electrolyte balance was carried out in 33 patients between the ages of 1 month and 18 years who underwent diagnostic cardiac catheterization and angiocardiography. Thirteen patients were under 1 year of age and 14 were cyanotic. A total of 53 individual studies were performed, with 20 patients undergoing 2 angiocardiographies. Serum sodium, chloride, potassium, bicarbonate, osmolality, blood urea nitrogen, pH, hemoglobin and hematocrit were measured immediately before the injection of Hypaque-M 75 per cent and within 5 minutes after, and at 15, 30, and 180 minutes thereafter. The study revealed a sharp rise in the serum osmolality with a similar sharp fall in the hematocrit and the pH. These findings suggest a marked dilutional and acidotic effect occurring within 5 minutes of injection. These changes were profound and it is suggested that more than 20 minutes should be allowed between angiocardiographies, if repeated studies are to be carried out, in order to allow for a recovery period from the acute biochemical insult produced by contrast media upon fluid and electrolyte balance.

Herman Grossman, M.D.
Department of Radiology
The New York Hospital-Cornell Medical Center
525 East 68th Street
New York, New York 10021

REFERENCES

1. Altman, A. R., Kahn, R. E., and Borrelli, F. J. Fifty per cent sodium diatrizoate for selective angiocardiography in infants. *Angiology*, 1967, *18*, 150–155.

2. Cotrim, E. S. Cardiac, blood pressure and respiratory effects of some contrast media: dangers of over-dosage. *Acta radiol.*, 1954, *44*, 58–74.

3. Giammona, S. T., Lurie, P. R., and Segar, W. E. Hypertonicity following selective angiocardiography. *Circulation*, 1963, *28*, 1096–1101.

4. Kloster, F. E., Bristow, J. D., Jacobs, W. R., Porter, G. A., and Griswold, H. E. Hemodynamic effects of angiocardiography. *Invest. Radiol.*, 1966, *1*, 398–406.

5. Marshall, M., and Henderson, G. A. Tendency to acidosis following injection of radio-opaque contrast material. *Brit. J. Radiol.*, 1968, *41*, 190–192.

6. Sotos, J. F., Dodge, P. R., Meara, P., and Talbot, N. B. Studies in experimental hypertonicity. I. Pathogenesis of clinical syndrome, biochemical abnormalities and cause of death. *Pediatrics*, 1960, *26*, 925–938.

7. Sotos, J. F., Dodge, P. R., and Talbot, N. B. Studies in experimental hypertonicity. II. Hypertonicity of body fluids as cause of acidosis. *Pediatrics*, 1962, *30*, 180–193.

CORONARY ARTERIOGRAPHY IN HYPERCHOLESTEROLEMIC PATIENTS*

By HAROLD A. BALTAXE, M.D.,† KURT AMPLATZ, M.D.,† RICHARD L. VARCO, M.D., PH.D.,‡ *and* HENRY BUCHWALD, M.D., PH.D.‡§
MINNEAPOLIS, MINNESOTA

BUCHWALD and co-workers[1–4] at the University of Minnesota Hospitals have shown that a partial ileal bypass operation markedly decreases the absorption and reabsorption of cholesterol and bile salts from the intestinal tract, thereby producing a substantial reduction in the circulating cholesterol levels.

In order to study the effectiveness of this procedure, not only on the lipids but on the patient's atherosclerotic status, functional and anatomic studies were performed prior to operation and have been repeated at periodic intervals thereafter. It is the purpose of this report to review the roentgenographic results in this group of patients and attempt to correlate these findings with clinical history, cholesterol levels, electrocardiography, vectorcardiography and double Master's excercise electrocardiography. To our best knowledge this represents the first and largest systematic angiographic study of patients with hypercholesterolemia.

MATERIAL

The ileal bypass program for hypercholesterolemia is now 5 years old. To date, approximately 100 patients have been evaluated for ileal bypass and 50 of these were selected for the procedure. A requirement for surgery was an elevated serum cholesterol level after at least 3 months of dietary management. The majority of these patients had clinical manifestations of progressive atherosclerosis, *e.g.*, myocardial infarctions, angina pectoris, claudications, cerebrovascular symptoms, etc. Some of them were completely asymptomatic and surgery was performed on the basis of elevated lipids and a family history of early deaths from coronary infarction. The patients have been less than 60 years of age and the majority were between the ages of 30 and 40 years. The youngest was 13 years old at the time of his operation. Nineteen of the 50 patients were females. Thirty-three patients in the current series had coronary angiography; at the initiation of the study program only aortography and femoral arteriography were performed.

METHODS OF EXAMINATION AND PROTOCOL OF STUDY

The sequential protocol of patient evaluation included hematologic values, serum electrolytes, serum proteins, serum uric acid, vitamin B_{12} absorption, serum carotene, serum vitamin A, and a total lipid profile (serum cholesterol, serum phospholipids, serum triglycerides, total serum lipids, serum lipoprotein electrophoresis, serum lipoprotein ultracentrifugation). Electrocardiography, vectorcardiography, double Master's exercise tolerance tests, and angiography were also performed.

In this report we shall present an evaluation of the roentgenographic findings and attempt to: (1) correlate coronary angiographic results with electrocardiography, vectorcardiography and double Master's electrocardiography; (2) correlate the angiographic findings and the preoperative cholesterol levels; (3) correlate the angiographic findings with aortography and femoral arteriography in the same patient; and (4) evaluate the sequential angiographic findings in the years following the bypass operation.

* Presented at the Sixteenth Annual Meeting of the Association of University Radiologists, Columbus, Ohio, May 8–11, 1968.
From the Departments of Radiology,† and Surgery,‡ University of Minnesota Hospitals, Minneapolis, Minnesota.
Supported by NIH Grants # HE 06314-04 HE 06314-07, and HE 11901-01 (5GYB), and the American Heart Association Grant 67 825.
§ Established Investigator, American Heart Association.

Table I

CORRELATION BETWEEN ELECTROCARDIOGRAPHIC FINDINGS AND APPEARANCE OF THE CORONARY ARTERIES

Total number of electrocardiograms 50
Total number of electrocardiograms on patients with coronary angiograms 33

Good Correlation		Bad Correlation	
Moderate to severe disease + positive electrocardiogram	Negative angiogram + negative electrocardiogram	Moderate to severe disease + negative electrocardiogram	Negative angiogram + positive electrocardiogram
12	4	15	2

The selective coronary arteriography was performed as previously described by Wilson *et al.*[5] via transfemoral percutaneous catheterization. Pre-shaped polyurethane catheters* were selectively inserted into the coronary arteries and 10 ml. of 60 per cent methylglucamine diatrizoate was injected manually into each coronary ostium. Biplane angiography was utilized with intermittent exposure, 3 per second, using a cut film changer. In some patients additional cinecoronary arteriography was performed.

The severity of coronary artery disease on angiography was classified as mild if the narrowing was less than 25 per cent, moderate if the narrowing was up to 50 per cent, and severe whenever the narrowing was over 50 per cent. Diffuse narrowed vessels were rated as being severely affected. This is somewhat different from the classification utilized by Wilson and associates.[5]

* Cordis Corporation, Miami, Florida.

RESULTS

Correlation of the coronary roentgenographic changes with electrocardiographic findings. All of the 50 patients had electrocardiography. Thirty-three also had coronary angiography. In 16 patients, the electrocardiographic findings correlated with the angiographic results in indicating the presence or absence of coronary disease. However, in 15 cases the electrocardiograms were negative, whereas the coronary arteriograms were interpreted as being abnormal. In this study we have not attempted to correlate specific anatomic areas of myocardial infarction present on the electrocardiogram with a specific occlusion on the coronary angiogram (Table 1).

Correlation between double Master's exercise electrocardiography and coronary angiography. Forty-four patients had double Master's electrocardiography. Of these, 28 had selective coronary arteriography. The roentgenographic findings corresponded fa-

Table II

CORRELATION BETWEEN DOUBLE MASTER'S TEST AND APPEARANCE OF THE CORONARY ARTERIES

Total number of Master's performed 44
Total number of Master's performed on patients with coronary angiograms 28

Good Correlation		Bad Correlation	
Moderate to severe disease + positive Master's	Negative angiogram + negative Master's	Moderate to severe disease + negative Master's	Negative angiogram + positive Master's
13	3	11	1

TABLE III

CORRELATION BETWEEN VECTORCARDIOGRAPHIC FINDINGS AND THE APPEARANCE OF THE CORONARY ARTERIES ON THE ANGIOGRAM

Total number of vectorcardiograms 45
Total number of vectorcardiograms in patients who were examined by coronary angiography 31

Good Correlation		Bad Correlation	
Moderate to severe disease + positive vectorcardiogram	Negative angiogram + negative vectorcardiogram	Moderate to severe disease + negative vectorcardiogram	Negative angiogram + positive vectorcardiogram
17	2	9	3

TABLE IV

CORRELATION BETWEEN CHOLESTEROL VALUES AND SEVERITY OF THE DISEASE IN THE CORONARY ARTERIES

Cholesterol values up to 400 mg. per cent				Cholesterol values above 400 mg. per cent			
Negative	Mild	Moderate	Severe	Negative	Mild	Moderate	Severe
3	2	1	14	2	2	1	8

TABLE V

CORRELATION BETWEEN ANGINA PECTORIS AND ANGIOGRAPHIC FINDINGS

Good Correlation		Bad Correlation	
Pain + positive angiograms	No pain + negative angiograms	No pain + positive angiograms	Pain + negative angiograms
18	6	8	1

vorably with the results of the Master's electrocardiograms in 16 cases. However, a negative double Master's examination was obtained in 11 cases where the angiographic findings were positive (Table II).

Correlation of vectorcardiography with coronary angiography. Forty-five patients had vectorcardiography performed. Of these 31 had selective coronary angiography. In 19 patients good correlation existed between vectorcardiography and coronary angiography. In 12 cases, however, no correlation was found. Of these cases 9 patients had negative vectorcardiograms but positive angiographic findings (Table III).

Correlation between roentgenographic findings and the preoperative cholesterol values. The patients who had coronary angiography were divided into those with preoperative serum cholesterols up to 400 mg. per cent

FIG. 1. Femoral arteriogram obtained in 1963 on a patient with high levels of serum cholesterol. An atherosclerotic plaque is seen to involve the vessel. (*B*) The same study 5 years later demonstrates the lack of progression in the extent of the plaque.

(20) and those with preoperative serum cholesterols over 400 mg. per cent (13) (Table IV). Of those who had values lower than 400 mg. per cent, 14 presented severe changes on angiography, whereas 1 had moderate changes. Two had mild changes and 3 patients had normal angiograms. Of the patients with preoperative cholesterol values over 400 mg. per cent, severe changes were found angiographically in 8 patients, moderate changes in 1 patient, mild changes in 2 patients, and negative findings in 2 patients. Thus, there appears to be no predictable difference in the coronary angiographic findings as a function of the relative preoperative serum cholesterol value, if the cholesterol concentration is initially elevated (roughly defined as over 250 mg. per cent).

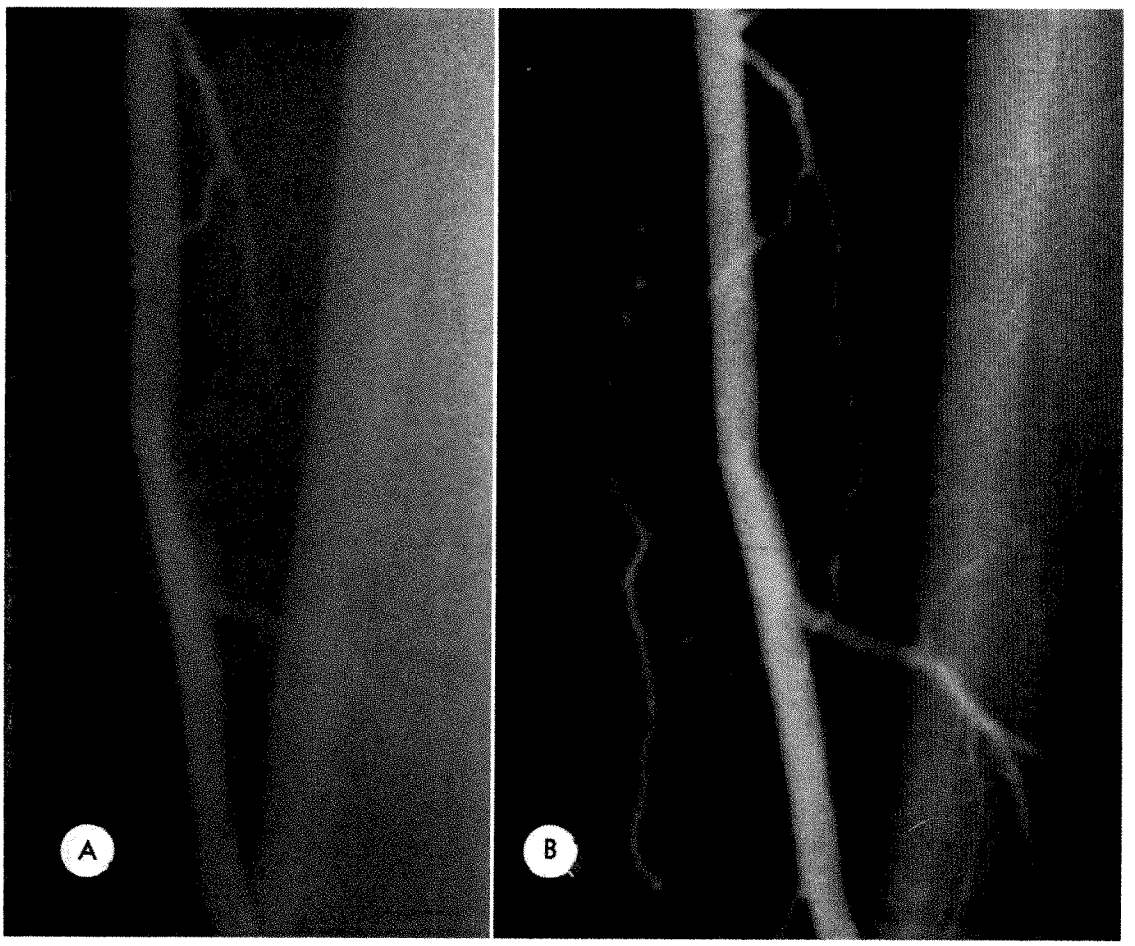
Correlation between roentgenographic find-

TABLE VI

CORRELATION BETWEEN FEMORAL ARTERIOGRAMS, AORTOGRAMS AND CORONARY ANGIOGRAMS

Total number of femoral arteriograms 23
Total number of femoral arteriograms in patients who had coronary angiograms 11

Good Correlation	
Aorta severely involved, coronary arteries severely involved	Aorta free of disease, coronary arteries free of disease
7	1
Bad Correlation	
Aorta severely diseased, coronary arteries free of disease	Aorta not diseased, coronary arteries diseased
0	3



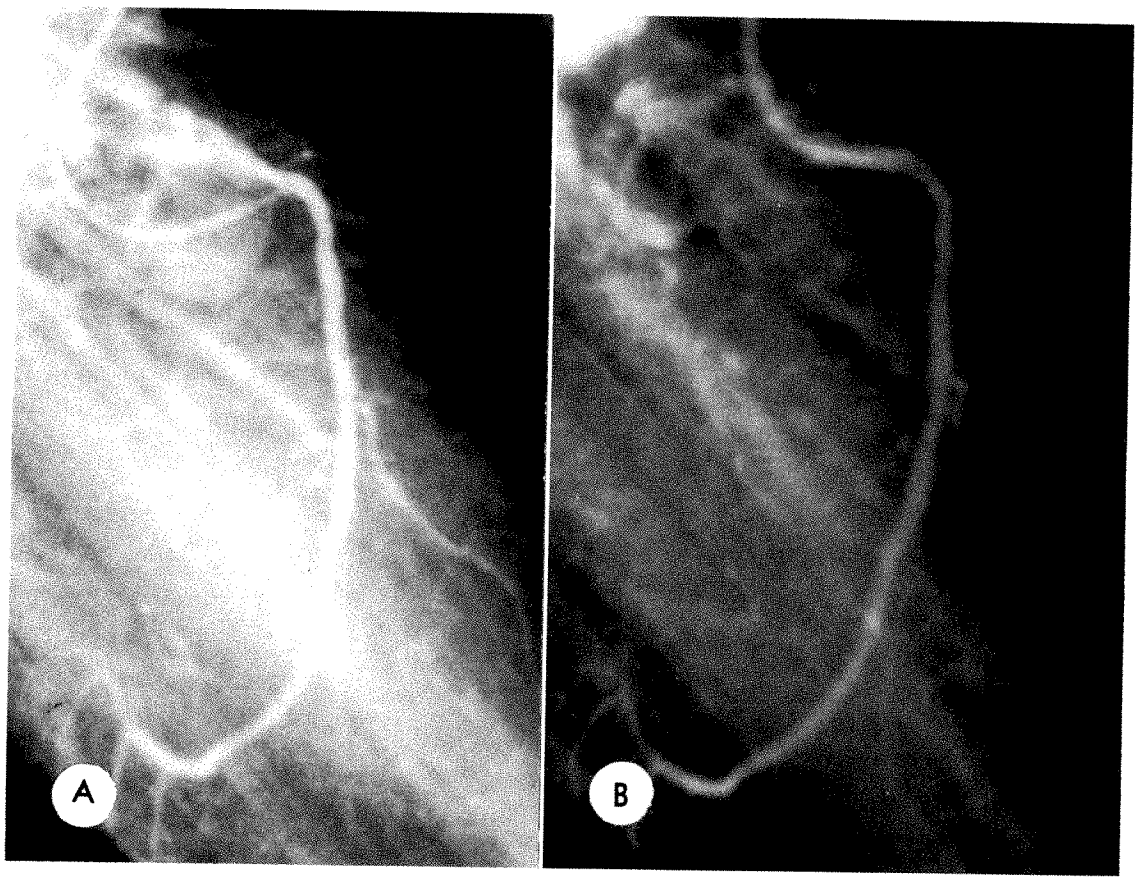


FIG. 2. (*A*) Lateral projection of a right coronary angiogram. The outline of the vessel is irregular and a diffused plaque formation is noted. (*B*) A 2 year follow-up study seems to indicate a more regular outline of the wall of the vessel and suggests regression of the disease.

ings and preoperative symptomatology. Of the 33 patients with selective coronary angiography, 24 presented good correlation between the severity of the roentgenographic findings and their clinical symptomatology. However, in 9 patients there was no pattern of angina pectoris, yet the patients had positive coronary angiograms (Table v).

Correlation between coronary angiography and peripheral arteriographic studies. Twenty-seven aortographies and femoral arteriographies were performed in this group of patients. Of these, 23 patients had coronary angiographies. In 7 cases, severe changes in the coronary tree correlated with severe changes in the aorta, iliac, and femoral arteries. In no case did the atherosclerotic process involve the aorta more severely than the coronary arteries. But, in 3 cases, the atherosclerotic process involved the coronary arteries more severely than the aorta and its major divisions (Table vi).

Arteriographic changes subsequent to the ileal bypass procedure. Follow-up selective coronary angiographies and/or peripheral arteriographies have been performed in all of the patients every 2 years following their operation. Throughout this period, no progression of the atherosclerotic process, as defined by the appearance of new plaques or the visible enlargement of old ones, was observed. Examples of preoperative and 2 and 5 year postoperative femoral arteriograms are shown in Figure 1, *A* and *B*. It has been our impression, although we hasten to add that this may be the result of differences in technique only, that in some

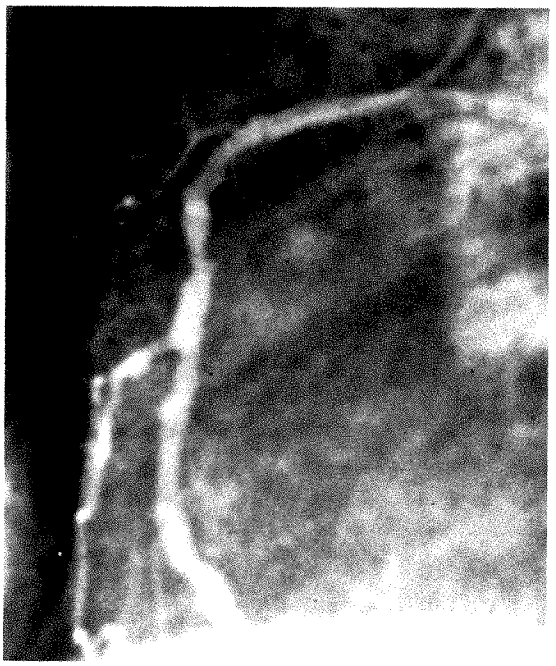


FIG. 3. An anteroposterior projection of a right coronary angiogram showing diffused atherosclerotic disease. This patient had a negative electrocardiogram, vectorcardiogram, and double Master's exercise electrocardiogram test.

of the follow-up examinations there appears to be some improvement in the roentgenographic pattern, as manifested by greater luminal diameter, decreased tortuosity, and decreased prominence in plaques. In Figure 2, *A* and *B* an example of possible improvement may be seen on comparison of the preoperative with the 2 year postoperative right coronary angiograms of a 44 year old physician.

DISCUSSION

It can be seen from this brief and preliminary evaluation that the vectorcardiogram seems to correlate better with the coronary angiogram than the 12 lead electrocardiogram, or possibly even the double Master's exercise tolerance test. However, all of these tests may remain negative, whereas the coronary angiogram demonstrates severe disease (Fig. 3). Given a hypercholesterolemic patient, his serum cholesterol did not serve as an indicator of the severity of his disease as seen in the

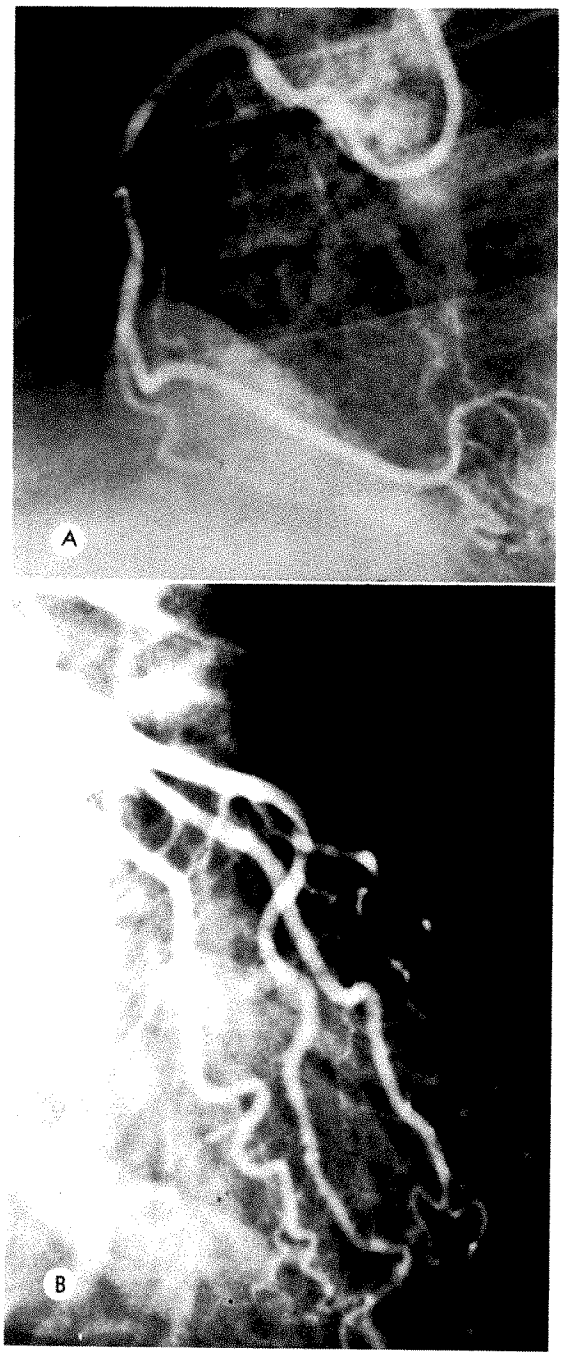


FIG. 4. (*A* and *B*) Anteroposterior projections of right and left coronary arteries in a 41 year old patient who had cholesterol levels up to 400 mg. per cent and whose electrocardiogram and vectorcardiogram suggested an old diaphragmatic myocardial infarction. This is a negative angiographic study.

case of H. W. who had normal angiographic and positive electrocardiographic findings (Fig. 4, *A* and *B*). Although angina pectoris is difficult to define, it would appear from our study that a history of exertional chest pain was well correlated with the angiographic findings of anatomic disease in the coronary tree. Since most of our patients were in the younger age group and the manifestations of their disease were primarily in the coronary vessels, it would seem that the atherosclerotic cardiovascular process generally starts as coronary artery disease. The preliminary data show no visible progression of atherosclerotic disease following ileal bypass, but the time of observation is only, at the most, 5 years, and definite conclusions cannot be made at this time. Furthermore, the possibility of reversal of the atherosclerotic process after ileal bypass is suggested, but is not conclusively demonstrated in this preliminary study. It should be noted, however, that peripheral cholesterol deposits have decreased as documented by the disappearance and decrease in size of periorbital xanthelasma, cutaneous xanthomata, and tendon xanthomata.

SUMMARY

The angiographic findings of 50 patients with hypercholesterolemia undergoing partial ileal bypass operation were analyzed. The angiographic findings were correlated with the electrocardiograms, double Master's exercise electrocardiograms, and vectorcardiograms. The best correlation with coronary angiography of these 3 modalities may be the vectorcardiogram.

Coronary angiography appeared to correlate well with the clinical symptomatology of angina pectoris.

The severity of atherosclerotic coronary artery disease in hypercholesterolemic patients did not correlate with the relative preoperative serum cholesterol level, *i.e.*, the degree of disease in patients with preoperative serum cholesterols below 400 mg. per cent was as severe as those with preoperative serum cholesterols above 400 mg. per cent. Evaluation in the same patient of peripheral arteriograms and coronary angiograms seems to indicate that atherosclerotic disease of the coronary arteries is often more pronounced and may precede disease of the aorta, iliac, and femoral arteries.

Sequential analysis of selective coronary angiography and peripheral arteriography in patients subsequent to ileal bypass has, in the 5 years of study, shown no visible progression of the disease process, and has suggested possible regression in 1 or 2 patients.

Harold A. Baltaxe, M.D.
Department of Radiology
University of Minnesota Hospitals
Minneapolis, Minnesota 55455

We are indebted to Doctor Naip Tuna for the electrocardiographic, vectorcardiographic, and double Master's electrocardiographic readings.

REFERENCES

1. BUCHWALD, H. Lowering of cholesterol absorption and blood levels by ileal exclusion: experimental basis and preliminary clinical report. *Circulation*, 1964, *29*, 713–720.
2. BUCHWALD, H., and GEBHARD, R. Effect of intestinal bypass on cholesterol absorption and blood levels in rabbit. *Am. J. Physiol.*, 1964, *207*, 567–572.
3. BUCHWALD, H., and VARCO, R. L. Partial ileal bypass for hypercholesterolemia and atherosclerosis. *Surg., Gynec. & Obst.*, 1967, *124*, 1231–1238.
4. BUCHWALD, H., and GEBHARD, R. L. Localization of bile salt absorption *in vivo* in rabbit. *Ann. Surg.*, 1968, *167*, 191–198.
5. WILSON, W. J., LEE, G. B., and AMPLATZ, K. Biplane selective coronary arteriography via percutaneous transfemoral approach. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1967, *100*, 332–340.

EFFECTS OF IONIZING RADIATION UPON THE IMMATURE RABBIT LARYNX*

By FREDERICK J. BONTE, M.D.,† VERNIE L. STEMBRIDGE, M.D.,‡ *and* JAMES D. REEF, M.D.†§
DALLAS, TEXAS

RECENTLY, while studying the problem of thyroid cancer in childhood,[1] we became interested in the theoretical and actual consequences of delivering large doses of ionizing radiation, in the course of radiotherapy, to the immature larynx in infancy and childhood. We have found that a surprisingly small amount of information is available in the literature. One paper, written long ago by Clerf,[2] described 4 cases of laryngeal hypoplasia and stricture in children as a consequence of very high dose intracavitary irradiation of the larynx with radium sources. No additional useful data were available from Winship,[4] who heads the Childhood Thyroid Cancer Registry, nor did Schweisguth,[3] of the Gustave-Roussy Institute, have any information concerning laryngeal abnormality secondary to irradiation of the thyroid region in children. Likewise, there were no pertinent laboratory investigations. We therefore undertook an experimental study to determine whether doses of ionizing radiation in the radiotherapeutic range might affect growth and development of the mammalian larynx.

MATERIAL AND METHOD

The animals used for this study were 45 weanling albino laboratory rabbits (about 6 weeks of age). Seven of the baby rabbits were designated as juvenile controls. They were weighed and sacrificed, and their larynxes were removed. The larynxes, stripped of thyroid tissue and hypopharyngeal mucosa, were measured in three dimensions and weighed. They were then fixed in 10 per cent formalin, embedded, sectioned transversely and stained for histologic study.

Twenty-seven rabbits were anesthetized with intravenous nembutal and were given laryngeal irradiation through a 3×3 cm. anterior neck portal with a 250 kvp. unit, with 0.5 mm. Cu, 1.0 mm. Al added filtration (1.8 mm. Cu half-value layer). Target-to-skin distance was 40 cm., and the dose rate was 148 r per minute in air at the level of the entrance skin. Five animals received a single exposure dose of 800 r; 10 animals received a single dose of 1,480 r; and 12 animals received a single dose of 1,924 r. Eleven rabbits were maintained as experimental controls, receiving both anesthesia and simulated irradiation.

Experimental and control animals were returned to their cages, and were fed thereafter on a normal laboratory diet. They were observed as closely as possible for evidence of illness, and for death. All surviving control and experimental animals were sacrificed 6 months after the date of irradiation, at which time they were about $7\frac{1}{2}$ months of age. The animals were weighed, and their larynxes were removed. The larynxes were measured, weighed and submitted to the same histologic examination as the juvenile controls.

RESULTS

All five rabbits which received single doses of 800 r to the laryngeal region survived for 6 months. Three of the larynxes were of normal weight and size (Table 1), but 2 of them were near the lower limits of the normal range. Histologically, each of these two small larynxes showed evidence

* Presented at the Sixteenth Annual Meeting of the Association of University Radiologists, Columbus, Ohio, May 8–11, 1968.
From the Departments of Radiology,† and Pathology,‡ The University of Texas Southwestern Medical School at Dallas, Dallas, Texas.
§ Research Trainee in Radiation Therapy, USPHS Training Grant CA 05136. The work described herein was supported by this Grant.

TABLE I

MEAN AND RANGE OF LARYNGEAL WEIGHTS FOR JUVENILE AND EXPERIMENTAL CONTROL RABBITS

Animal Group	No.	Survived (6 mo.)	Larynx Weight (mg.) Mean	Range	Pathologic Changes* Chond.	Sq. Metap.	M.G. A.
Juvenile Controls	7	—	460	280–650	—	—	—
Experimental Controls	11	11	1,005	800–1,295	—	—	—
Treated Group							
800 r	5	5	990	820–1,080	2/5	1/5	0/5
1,480 r	10	9	770	520–915	3/9	8/9	1/9
1,924 r	12	6	780	680–1,050	3/6	6/6	3/6

* The experimental groups which received laryngeal exposure doses of 800 r, 1,480 r, or 1,924 r of x-radiation are analyzed for survival, for mean and range of laryngeal weight at sacrifice, and for the incidence of histologic changes, including chondromalacia (Chond.); metaplasia of the normal stratified, ciliated columnar epithelium to a stratified squamous cell type (Sq. Metap.); and atrophy of mucous glands (M.G.A.), among animals in each group which survived until sacrificed 6 months after irradiation.

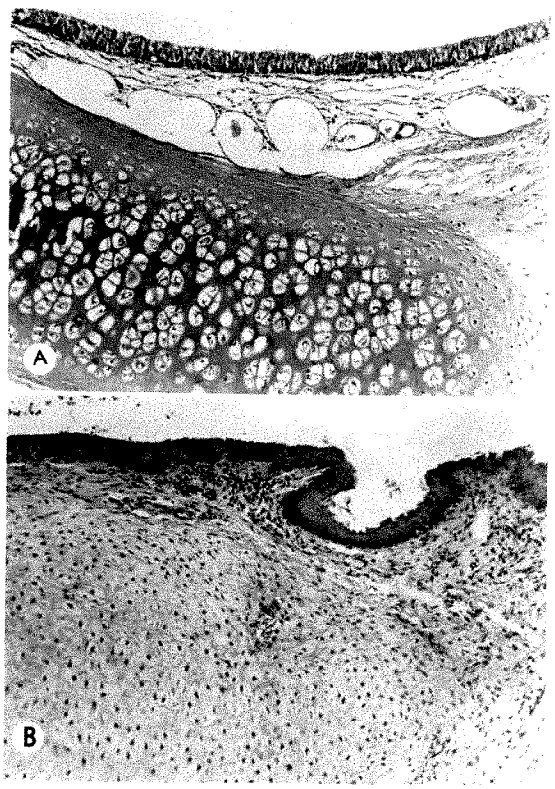


FIG. 1. (*A*) Transverse section of the larynx of a 7½ month old control rabbit made through the thyroid cartilage. Note normal, orderly cell columns and normal stratified, ciliated columnar lining epithelium. (Stained with hematoxylin and eosin; 150×.) (*B*) Transverse section of the larynx through the thyroid cartilage; specimen was obtained from a 7½ month old rabbit which had received an exposure dose of x-radiation of 1,480 r at the age of 6 weeks. Note disorganization of cartilage cell columns and immaturity of chondrocytes in a pattern of chondromalacia. There is metaplasia of lining epithelium from the normal columnar to a stratified squamous cell type. (Stained with hematoxylin and eosin; 150×.)

of patchy metaplasia of the normal stratified, ciliated columnar epithelium to a stratified squamous cell type. In addition, there was evidence of chondromalacia, with immaturity of cartilage cells, and disarray of cartilage cell columns (Fig. 1, *A* and *B*).

Nine of the 10 rabbits which received single doses of 1,480 r to the laryngeal region survived for 6 months (Table 1). One died at 5 months of unknown causes, but at autopsy autolysis was too far advanced to permit appraisal of the histologic condition of the larynx. The larynxes of the remaining animals in this group were generally lower in weight than normal, and histologically showed a marked tendency toward replacement of the normal columnar (Fig. 1*A* and 2*A*) by a stratified squamous cell epithelium (Fig. 1*B* and 2*B*). Several of the larynxes showed evidence of mucous gland atrophy (Fig. 2, *A* and *B*). Three of the larynxes showed the changes of chondromalacia (Fig. 1*B*), and there was a scattering of other changes, such as evidence of focal acute and chronic infection, and granular change in the fibrocollagenous tissue.

Of the 12 animals which received single

laryngeal doses of 1,924 r, 6 died within 1 month after irradiation with signs of acute respiratory distress. In no case was an autopsy obtained soon enough to secure a larynx for examination which was free of significant autolysis. Five of the 6 surviving animals had larynxes at, or below, the lower limits of normal in size, when compared with the experimental controls (Table I). Histologically, mucous gland atrophy was common as were squamous cell epithelial metaplasia and chondromalacia.

As a matter of interest anteroposterior and lateral roentgenograms of the neck were made of both classes of control animals and of all experimental animals at sacrifice. As might be expected (Table II) there was a high incidence of cervical spine deformity, with the larger number of abnormalities occurring in the higher dose ranges. The commonest detectable abnormality was anterior wedging of the centra of C2, 3, or 4 (Fig. 3, *A* and *B*).

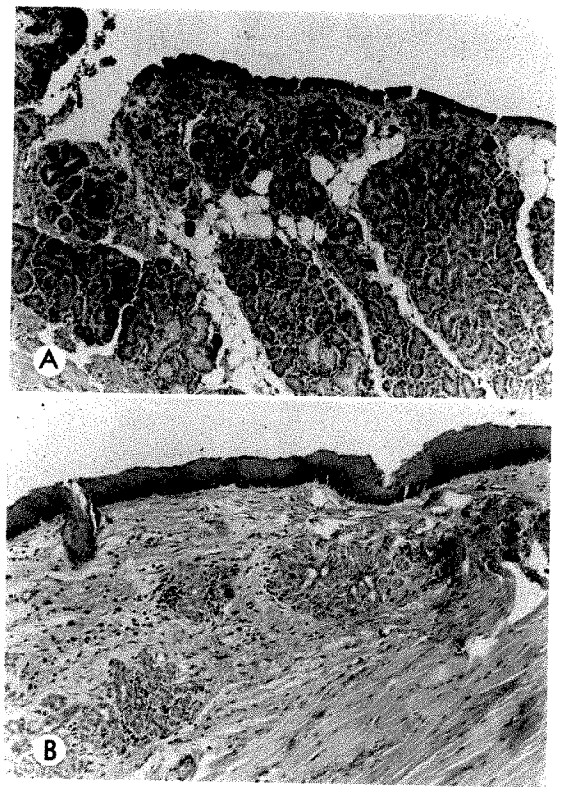


FIG. 2. (*A*) Transverse section of the larynx of a 7½ month old control rabbit shows abundance of richly cellular mucous glands. Note normal stratified, ciliated columnar epithelium. (Stained with hematoxylin and eosin; 150×.) (*B*) Transverse section of the larynx of a 7½ month old rabbit which had received an exposure dose of 1,924 r at the age of 6 weeks. Mucous glands are sparse, and metaplasia of normal columnar epithelium to a stratified squamous cell type has occurred. (Stained with hematoxylin and eosin; 150×.)

DISCUSSION

Although the adult rabbit seldom uses his larynx for phonation, its structure seems similar enough to that of the human to suggest that it is a good model for the purposes of this experiment. In general, it may be said that the principal gross effect of exposure of the immature rabbit larynx to tolerable tumor doses of ionizing radiation, biologically similar to those employed in human radiotherapy, was reduction in its eventual size. Weights of irradiated larynxes were in a lower range than those of controls, and in some instances it was possible to assign laryngeal undergrowth to chondromalacia. Squamous cell metaplasia,

TABLE II

INCIDENCE OF CERVICAL SPINE DEFORMITIES*

Animal Group	No.	Survived (6 mo.)	C-Spine Abnormality
Experimental Control	11	11	0/11
Treated Group			
800 r	5	5	1/5
1,480 r	10	9	6/9
1,924 r	12	6	5/6

* Incidence of cervical spine deformities among control and surviving experimental animals on roentgenograms made 6 months after anterior irradiation of the neck with stated exposure doses.

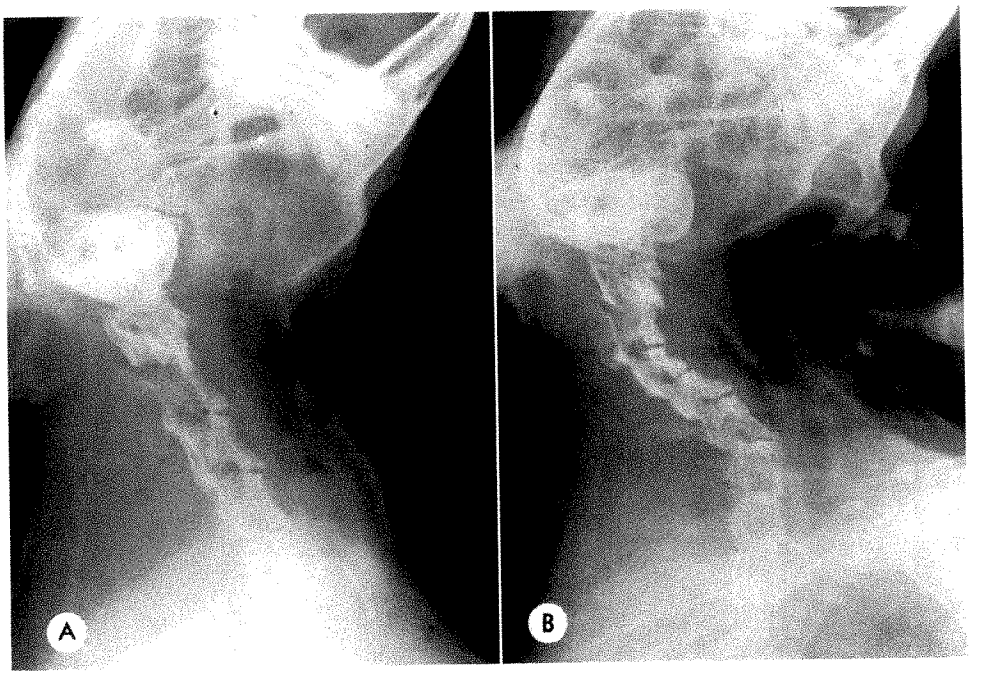


Fig. 3. (*A*) Lateral roentgenogram of the cervical region of a control rabbit 7½ months of age. The contours of the various elements of the cervical spine are normal. The larynx has been removed surgically. (*B*) Lateral roentgenogram of the cervical region of a 7½ month old rabbit which had received an anterior exposure dose of x-radiation of 1,480 r at the age of 6 weeks. Note reduction in altitude of the centra of C2, 3 and 4, with anterior wedging, most marked at C3. The larynx has been removed surgically.

mucous gland atrophy, and diffuse and focal chronic inflammation could not readily be separated from one another in a general picture of mucosal atrophy, which was most pronounced at the highest radiation doses.

CONCLUSIONS

Laryngeal hypoplasia may be produced by irradiating immature rabbit larynxes with single doses of 800 to 1,924 r—exposures biologically comparable to those which the larynxes of a number of children receiving external beam radiotherapy for carcinoma of the thyroid gland might have sustained. If the changes of hypoplasia have been produced in humans, they seem not to have been significant enough to give signs, or symptoms, or otherwise to have been noted in the appraisal of these cases in the several thyroid tumor registries. However, because of the possible late consequences of mucous membrane epithelial metaplasia, such as carcinogenesis, it would seem wise to ensure that a child who has had major radiotherapy in, or about, his larynx, be seen periodically by competent physicians for the rest of his life.

Frederick J. Bonte, M.D.
Department of Radiology
University of Texas
Southwestern Medical School at Dallas
5323 Harry Hines Boulevard
Dallas, Texas 75235

The authors wish to acknowledge the excellent technical assistance of John G. Moore, R.T., and Mrs. Carolyn Simon.

REFERENCES

1. Bonte, F. J. Radioiodine and child with thyroid cancer. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1965, *95*, 1–24.
2. Clerf, L. H. Laryngeal complications of irradiation. *Arch. Otolaryng.*, 1927, *6*, 338–345.
3. Schweisguth, O. Personal communication.
4. Winship, T. Personal communication.

VOL. 105, NO. 4

VASCULAR STRUCTURE OF GLIOBLASTOMAS*

By J. H. SCATLIFF, M.D.,† W. B. RADCLIFFE, M.D.,‡
H. H. PITTMAN, B.S.,§ *and* C. H. PARK, M.D.‖
CHAPEL HILL, NORTH CAROLINA

THE gross angioarchitecture of glioblastomas during life has been well documented by means of cerebral angiography. Little direct correlation, however, of *in vivo* tumor vascularity outlined by contrast material and postmortem identification of vessels has been made.[2,11]

The role that deep medullary veins may play in the formation of the vascular network draining the tumor has been recognized.[4] For the most part, tumor vessel analysis has remained descriptive and several classifications have been developed (Table 1).[10,15]

MATERIAL AND METHOD

In the last 5 years, 50 postmortem brain tumor vessel injections have been carried out. The technique of injection of a mixture of thorotrast and micropaque, equipment used, and methods of analysis have been described previously.[13] Twenty-six brains with astrocytomas of varying grades of malignancy (Kernohan classification[6]) have been studied. The specimens were investigated primarily by means of inspection of gross and microscopic preparations, as well as microradiographic films of sections ranging from 100 micra to 1.2 cm. in thickness. These, in turn, were compared with cerebral arteriograms which had been done in the majority of patients. Since surgery was seldom performed in this group of patients, the tumor vascularity was largely intact except in localized areas where a biopsy had been taken.

RESULTS

Glioblastoma tumor vessels appear to have two principal origins. The first group is derived from existing anatomic vessels taken over by the tumor for its arterial supply and venous drainage. These may be relatively large arteries or deep medullary and superficial veins, as shown in Figure 1, *A*, *B* and *C*; and 2. The vessels can remain of normal size or undergo varying degrees of dilatation secondary to increased blood flow through the tumor. The arteries involved may become tortuous, due possibly to more rapid blood flow or adjacent pressures of tumor growth, necrosis, or edema. It would appear that this type of vascular transformation is responsible for the coarser vessels, including the arteriovenous anastomoses, aneurysmal dilatation of vessels, and "sinusoids," described by Lorenz,[10] Wickbom,[15] and others.[14]

Of particular interest is the finding in several cases of hypervascularity of cortical gray matter involved by tumor (Fig. 3, *A*, *B* and *C*; 4; and 5, *A-D*). In each instance, the cortical arteries and veins have undergone dilatation and are better filled with contrast material than in areas of gray matter not infiltrated by tumor. It would appear that these vessels may not only dilate, as shown in histologic sections (Fig. 5, *C* and *D*), but also serve as progenerative vessels for the neocapillary circulation of the tumor. Similar vascular alterations can occur in the central gray matter as indicated in Figure 6, *A* and *B*.

It would appear that the diffuse homogeneous or nearly homogeneous blushing seen in cerebral arteriograms of some glioblastomas can be produced by this type of altered gray matter vascularity.

* Presented at the Sixteenth Annual Meeting of the Association of University Radiologists, Columbus, Ohio, May 8–11, 1968.
From the Department of Radiology, University of North Carolina School of Medicine, Chapel Hill, North Carolina.
† Professor of Radiology, University of North Carolina School of Medicine.
‡ Assistant Professor of Radiology, University of North Carolina School of Medicine.
§ Fourth-year Medical Student, University of North Carolina School of Medicine.
‖ Third-year Resident and Part-time Instructor of Radiology, University of North Carolina School of Medicine.
This study was supported in part by U. S. Public Health Service Grant B10-1050, United Medical Foundation of North Carolina, Inc. Grant 324-UNI-1 (276), and a grant from the Anna Fuller Fund, Yale University Medical School.

TABLE I

ARTERIOGRAPHIC CLASSIFICATION OF GLIOBLASTOMAS

Lorenz[10]	Type I	Finely granular, indistinctly outlined shadow of contrast material
	Type II	Groups of threadlike blood vessels which are intertwined and give pinhead sized contrast spots
	Type III	Arteriovenous anastomoses of varying size
Wickbom[15]	Type I	Irregular coursing vessels of varying size. Early filling of veins (arteriovenous fistulas)
	Type II	Irregular tumor vessels similar to those in Type I but no early filling of veins
	Type III	Shorter and smaller calibered vessels than Type I and II. Small aneurysmal dilatation of vessels present
	Type IV	Short, very thin vessels with irregular lumens
	Type V	Decreased vascularity in region of tumor. Tumor ringed by small irregular vessels and arched veins in some cases
	A highly vascular zone around a less extensive avascular area could be seen in varying numbers of cases in Types I, II, III, and IV	

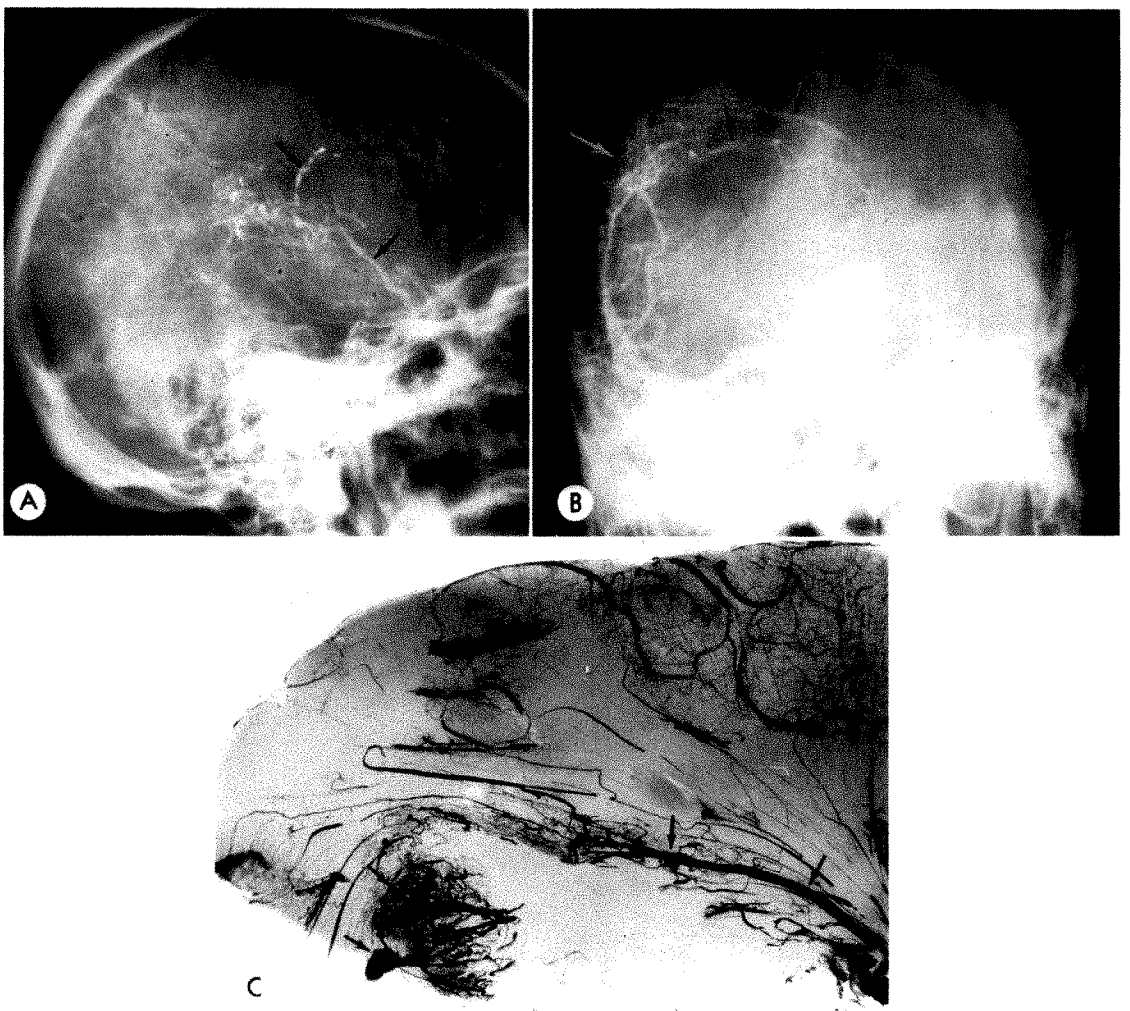


FIG. 1. Case 1. (*A*) Lateral *in vivo* arteriogram showing coarse, irregular vessels in astrocytoma, Grade III. Aneurysmal dilatation of vessels and early venous filling (arrows) are noted. (*B*) Frontal projection shows early venous filling (arrows). Faint tumor blush in the region of coarse middle cerebral vessels (white arrow) is seen. (*C*) A 6 mm. thick coronal section microradiograph can be correlated with the arteriogram in *B*. Arrows on right show a deep medullary vein seen in the arteriogram. Arrows on left show coarse vessels in framework of neocapillary circulation of tumor. X designates central necrosis in tumor.

The patient in Figure 3 exhibits a ring of uniform, faint vascular staining, which in postmortem sections can be attributed to the hypervascular gray matter involved by viable tumor which surrounds a large area of central necrosis. The deep-seated, cloud-like shadow seen in the arteriogram, shown in Figure 6*A*, correlated well with the increased and new vascularity found in the thalamus, which had been largely replaced by tumor.

A second group of vascular formations in glioblastomas are made up of new vessels induced by or developed for tumor growth. Although these vessels may spring from existing vessels, they assume bizarre configurations. Figure 7*A* shows patterns of wild tangles and irregular meshworks of vessels in viable portions of tumor, as well as infiltrative tumor in the corpus callosum (Fig. 7*B*).

In several cases, a rounded to spherical reticulum of tumor vessels, measuring 3–5 mm. in diameter, was found. Figure 8*A* illustrates one example of this type of formation seen in the viable tumor periphery of a temporal lobe glioblastoma. Detailed examination of the structure (Fig. 8*B*) showed what appeared to be a pedicle of veins and arteries which fanned out to encompass an island of tumor with areas of necrosis (Fig. 8*C*). Histologic sections (Fig. 8*D*) through the vascular margin about the tumor island showed the characteristic glomeruloid formation found in many glioblastomas.

A second example of a well-defined, rounded network of tumor vessels is shown in Figure 9. This structure, which measured approximately 5 mm. in diameter, was one of several similar groupings of tumor vessels in an astrocytoma, Grade IV. On histologic section, the central vessels were shown to have muscularized veins, indicating the presence of arteriovenous shunting in the formation. The vessels were in a viable portion of the tumor.

Another type of vascularity which may contribute to an arteriographic tumor blush is that produced by vessels arising in a necrotic area of a glioblastoma undergoing hyalinization. An example of this is shown in Figure 8*A*. The regular collection of vessels in the healing area are, in all probability, new vessels arising from residual tumor vessels left in the necrotic mass.



FIG. 2. Case II. Microradiograph of 6 mm. thick section of outer parietal brain. Dilated and tortuous contrast medium filled vessels are transcortical arteries and veins within a glioblastoma (astrocytoma, Grade IV).

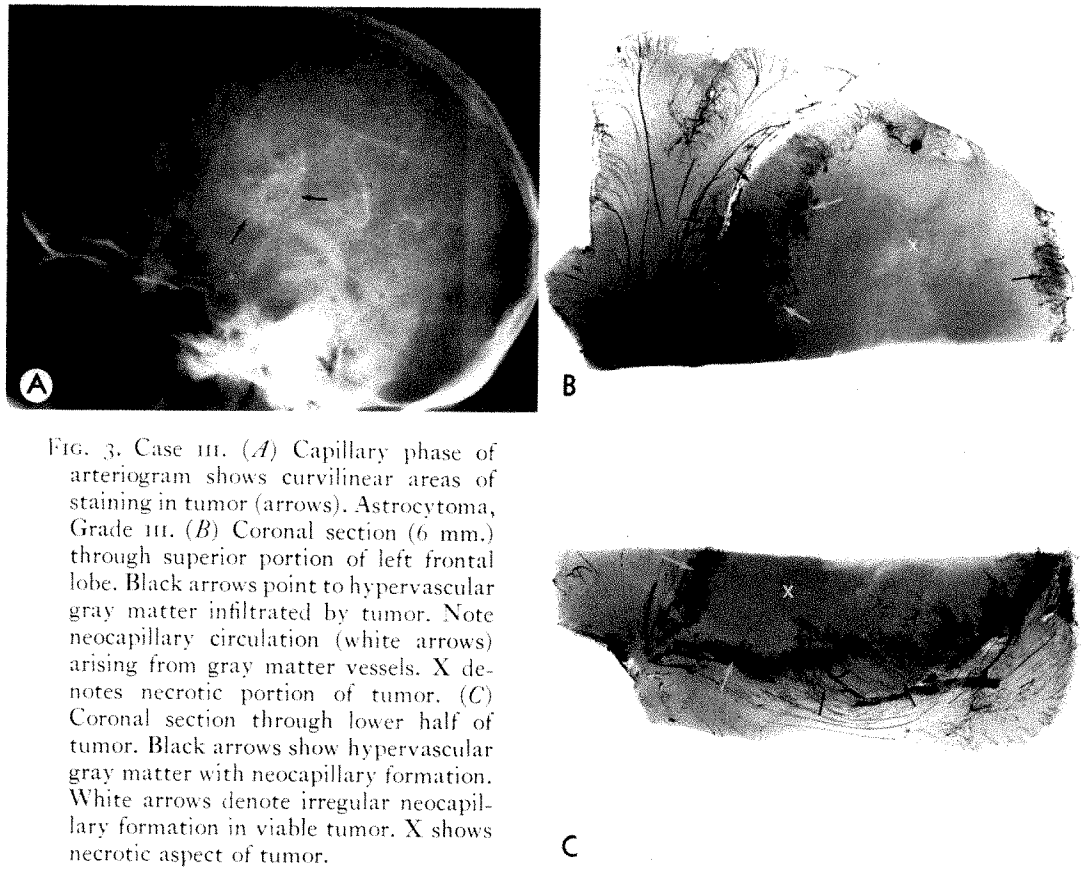


Fig. 3. Case III. (*A*) Capillary phase of arteriogram shows curvilinear areas of staining in tumor (arrows). Astrocytoma, Grade III. (*B*) Coronal section (6 mm.) through superior portion of left frontal lobe. Black arrows point to hypervascular gray matter infiltrated by tumor. Note neocapillary circulation (white arrows) arising from gray matter vessels. X denotes necrotic portion of tumor. (*C*) Coronal section through lower half of tumor. Black arrows show hypervascular gray matter with neocapillary formation. White arrows denote irregular neocapillary formation in viable tumor. X shows necrotic aspect of tumor.

DISCUSSION

A precise documentation of vessel origins and configurations in gliomas seems important from several standpoints. A knowledge of the constituent vascularity may aid in better recognition of the tumor in cerebral angiograms and assist in the differential diagnosis. This is particularly true as improved angiographic methods such as magnification arteriography, angiotomography, and subtraction gain more widespread use.



Fig. 4. Case IV. A 3 mm. coronal section through the temporal lobe gyri infiltrated by tumor (astrocytoma, Grade III). V designates sulcal vein draining dilated cortical veins. Neocapillary circulation is evident.

Research into the causes of the essentially lethal nature of a glioblastoma has been directed primarily toward a better understanding of the cellular biology of the tumor. These attempts are certainly necessary; however, a study of the vascularity of the tumor would appear equally important. The extensive spread through the brain of many glioblastomas must be fostered by the character of the anatomic vessels available to it, as well as the propensity of the tumor to generate new vessels. Insights gained into the vascular life of these tumors may be helpful in the planning of better techniques for surgical

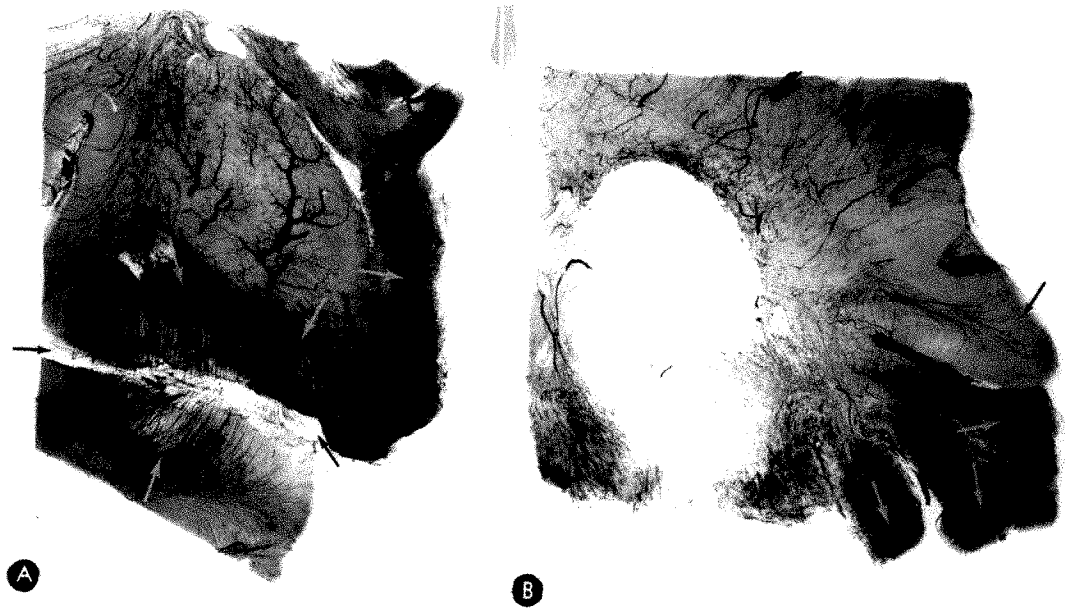


Fig. 5. Case v. (*A*) A 6 mm. coronal section through the frontotemporal region with tumor (astrocytoma Grade III) in both lobes. White arrows point to hypervascular gray matter with neocapillary circulation. Black arrows denote sylvian fissure. Tumor has grown across fissure. (*B*) White arrows denote hypervascularity in frontal lobe gray matter infiltrated by tumor. Black arrow designates gyrus with minimal tumor infiltration.

resection as well as the use of radiation and cytotoxic agents.

How does the glioblastoma derive its blood supply? Although at present specific information about this is lacking, it would seem most likely that this tumor behaves in the same manner as other already observed lesions. Lindgren[9] has indicated that tumor blood supply is induced from preexisting capillaries. He has noted that solid buds of vascular tissue spring from the capillaries and are incorporated in the

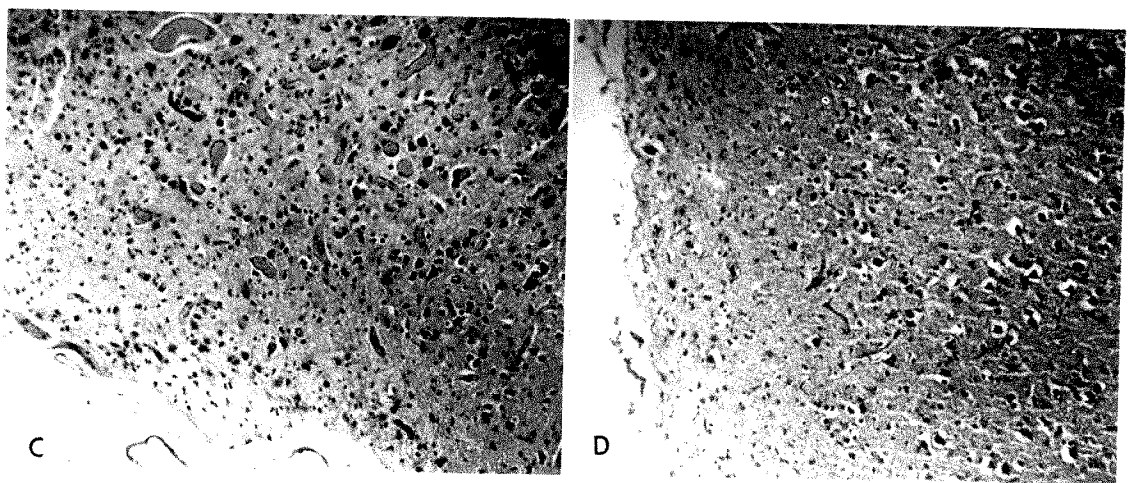


Fig. 5. (*C*) Histologic section (10 micra) of gray matter portion of gyrus with marked hypervascularity shown in *B*. Note dilatation of arteries and veins and extensive tumor involvement of all cortical layers. (*D*) Histologic section of gray matter of gyrus with minimal tumor infiltration, shown in *B*. Note lack of vessel dilatation as seen in *C*.

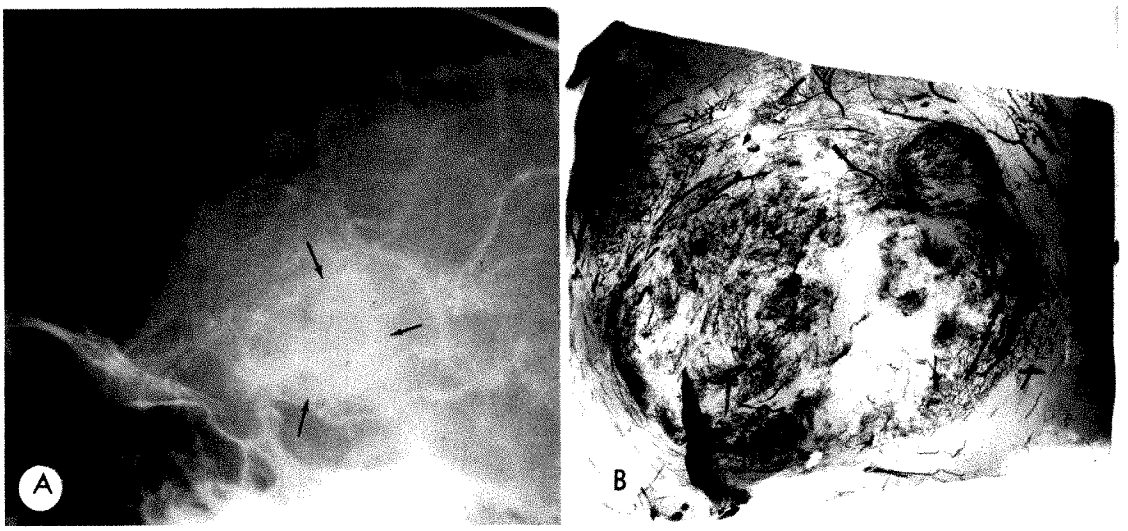


FIG. 6. Case VI. (*A*) Arteriogram shows homogeneous tumor stain (arrows) localized in region of thalamus. (*B*) A 3 mm. coronal section of thalamus shows marked increase in vascularity of vessels in gray matter and new capillary formation within tumor (astrocytoma, Grade IV).

tumor. At almost the same time, the new vascular appendages become canalized. In all probability, the rapid and disruptive growth in a capillary setting of this type promotes arterial and venous links of many different calibers. This process, in turn, establishes varying degrees of shunting within the tumor, as seen in cerebral arteriography and in specimen studies.

Does the site of origin of the glioblastoma influence the nature of its blood supply? It has been observed[5] that gray matter has a richer vascular supply than white matter in a ratio of 6:1 to 3:1. Reference to Figures 3, 4 and 5, wherein tumor infiltrating gray matter has invoked vasodilatation



FIG. 7. Case VII. (*A*) A 6 mm. coronal section of tumor (astrocytoma, Grade IV) in right frontal lobe. Irregular meshworks of new tumor vessels are seen. Avascular areas are necrotic. (*B*) Two 3 mm. coronal sections of corpus callosum showing irregular tumor vessels. Vascular connections have been established between pericallosal arteries (arrow, upper section) and septal vein (arrow, lower section).

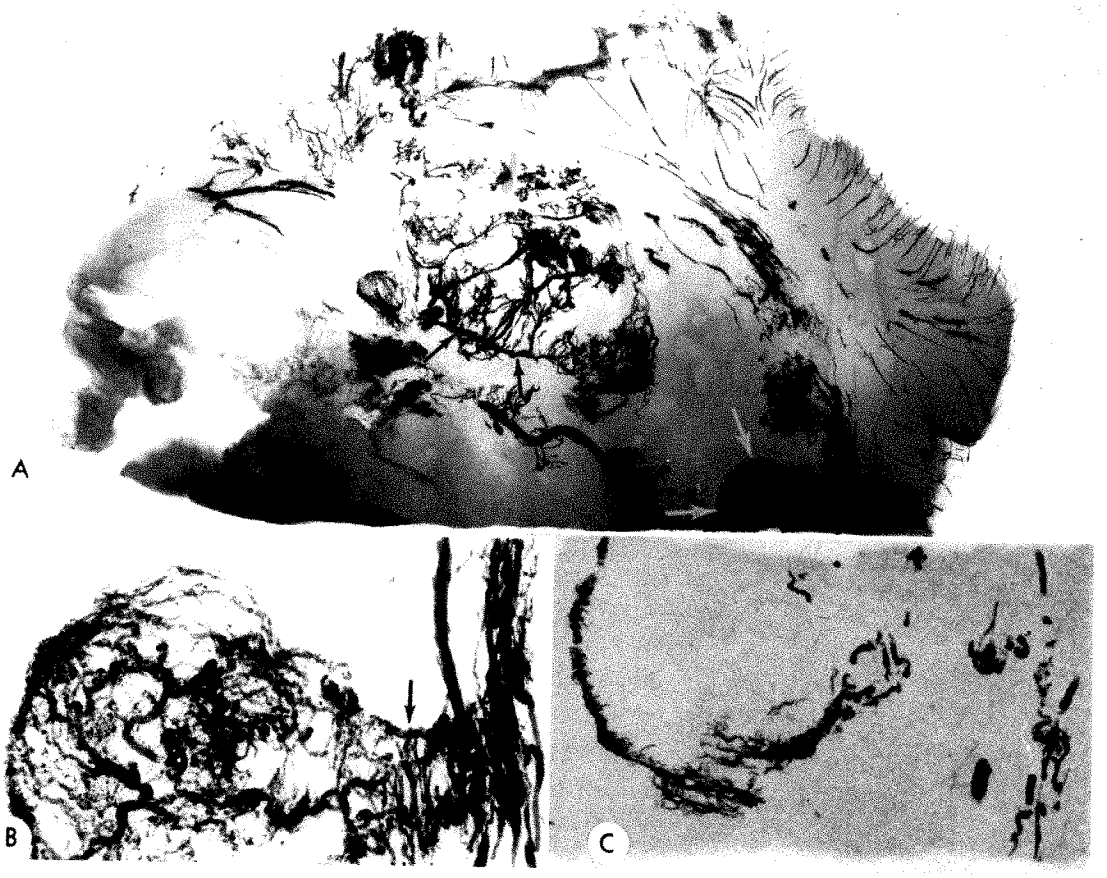


FIG. 8. Case VIII. (*A*) A 3 mm. coronal section through the temporal lobe with tumor (astrocytoma, Grade IV). White arrows denote spherical formation of new vessels around island of viable tumor. Black arrows show vessels in necrotic region of tumor undergoing hyalinization. (*B*) A 3 mm. thick section of spherical formation of vessels shown in *A*. The network is 4 mm. in diameter. Large vessels are arteries and veins connected to larger vessels through a vascular pedicle (black arrow). (*C*) A 240 micra section of formation showing central avascular area which on histologic sectioning showed viable tumor with areas of necrosis.

of gray matter arteries and veins, as well as abnormal branching of these vessels, would suggest that gray matter can contribute significantly to the vascular framework of the malignant glioma.

The increased gray matter vascularity seen in association with tumor infiltration is not unlike that observed in some brain infarcts.[12] This state, which has been termed "luxury perfusion,"[7] can be seen in cerebral arteriograms where a marked capillary blush outlining the infarcted brain gyri is noted. An intriguing question concerning the role that elevated pCO_2, associated with the infarct, may play in dilatation of gray matter vessels can be raised. Possibly a similar acidotic stimulus is created by rapid tumor growth within or adjacent to gray matter which is responsible for the vasocapillary dilatation noted in this layer. It is also interesting to speculate on the possible association of altered pH levels in brain tissue and the degree of neovascularity which may be induced from pre-existing vessels.

A further conjecture relates to the degree of malignancy of a glioblastoma and its involvement with gray matter. Possibly a glioma within white matter may remain dormant until gray matter infiltration occurs and a more vascular stroma becomes available for tumor growth. By the same

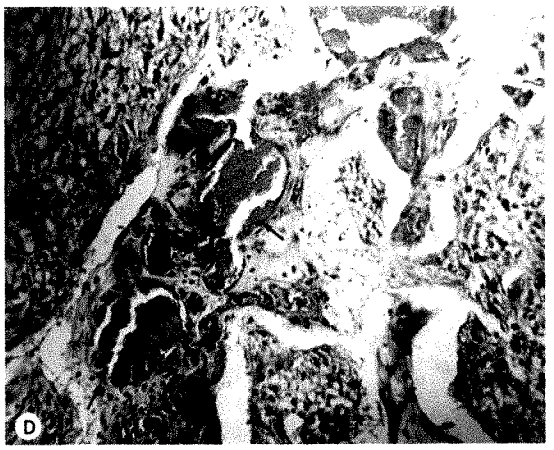


Fig. 8. (*D*) A 10 micra histologic section through contrast material filled vessels in margin of structure shown in *A*, *B* and *C* revealed glomeruloid formations (arrows) typical of glioblastomas.

token, a glioma arising within gray matter may become more rapidly malignant and infiltrate widely because of a richer gray matter blood supply.

Of interest is the observation made by Davidoff[1] that cerebellar astrocytomas have a much better prognosis than astrocytomas arising in the cerebral hemispheres. Seventy-seven per cent of the cerebellar astrocytomas in his series became cystic as compared with 29 per cent of the lesions in the cerebrum. Possibly available blood supply for tumor growth, or the lack of it, in the cerebellar lesions is the determining factor.

Although the number of glioblastomas showing a diffuse homogeneous blush in our series is limited, all of these on postmortem analysis showed increased gray matter vascularity and were highly malignant (astrocytoma, Grade III or IV). When a homogeneous blush is seen in cerebral arteriograms, and meningioma can be excluded, gray matter involvement by a glioma of advanced malignancy should be considered. It must be stated, however, that other lesions such as cerebral infarction and metastases can involve gray matter in the same way. Gyri may also be displaced by cerebral abscesses, as described by Heinz and Cooper.[3] If the gyrus is well visualized by contrast material in dilated cortical vessels, tumor vascularity may be mimicked. Glial reaction associated with the abscess may also have sufficient vascularity to produce a homogeneous stain on arteriography.

The small spherical networks of vessels surrounding islands of tumor with or without necrosis are of considerable interest. Perhaps the best explanation for this vascular configuration is the initial investment of a phalanx of growing tumor by newly formed capillaries. A similar process can be seen in tumor transplants in rabbit ears, as indicated by Ide and co-workers.[5] Capillaries surround the tumor 3 to 8 days after transplantation. With continued growth of the tumor, central necrosis occurs. Although extensive necrosis does occur, the vascular unit that has developed continues to function. Possibly the small vascular lacunae or aneurysms described in some glioblastoma arteriograms are due to contrast material filling networks of vessels in formations of this kind.

In all probability, the vascular network shown in Figure 9 has been formed in the same way as the structure described in the case shown in Figure 8*B*. The fact that histologic sections did not show necrosis in the center of the formation can be attributed possibly to a slower growth of tumor. The cerebral arteriogram of this case showed a faint, rounded area of



Fig. 9. Case IX. A 3 mm. thick section shows well-formed, 4 mm. in diameter, capillary network (arrows) in viable tumor (astrocytoma, Grade III). Histologic sections showed the formation to be a well-developed arteriovenous shunt.

staining which was similar to that of a small angioma.

Figure 10 summarizes the various vascular components of glioblastomas which have been identified in this postmortem survey of the injected tumors.

An experimental approach has recently been developed at our institution which would appear helpful for the study of blood vessel formation in glioblastomas. Figure 11 shows coronal sections of a guinea pig brain in which a human glioblastoma has been successfully transplanted and the tumor vessels filled with contrast material. It is hoped that this model system can be used to shed further light on the early development of vascularity in glioblastomas. It is possible that the importance of gray matter vascularity in determining the degree of glioblastoma malignancy may be established by this means.

SUMMARY

A series of postmortem injections of the blood supply of glioblastomas has been analyzed and correlated with *in vivo* cerebral arteriograms done in the majority of the tumors. The tumor vascularity has two origins. The first is that adapted from pre-existing circulation and consists of

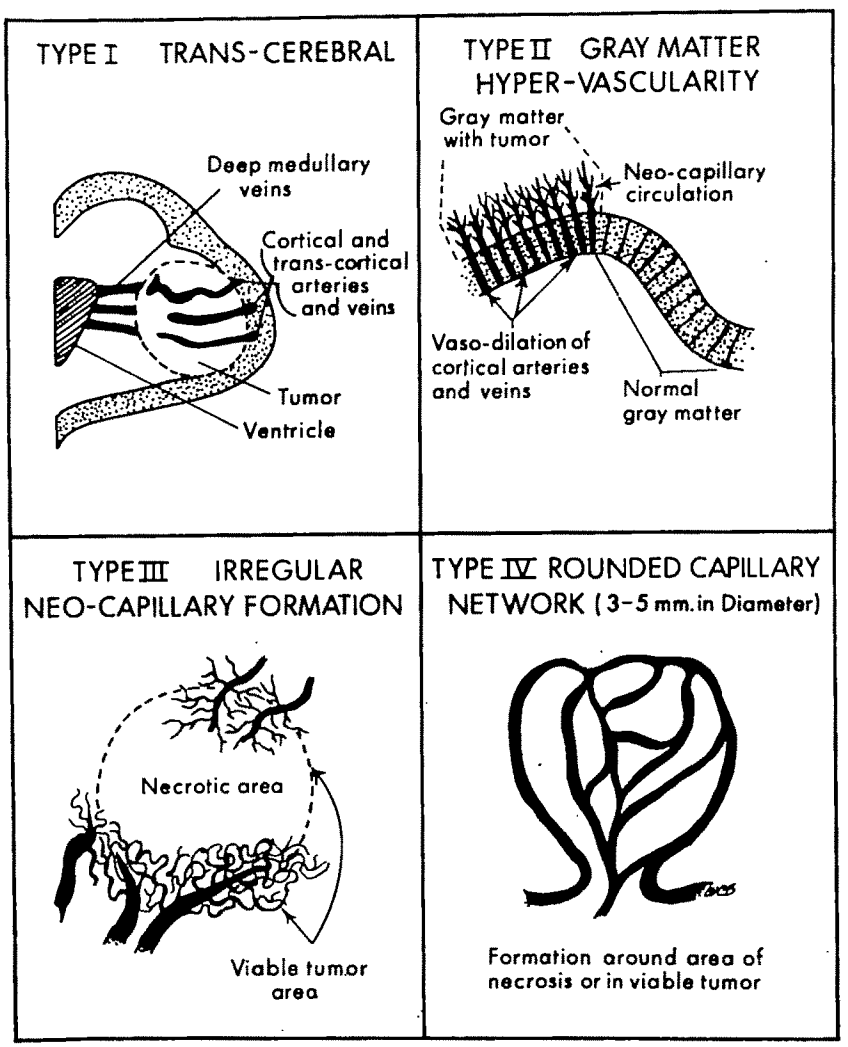


Fig. 10. Diagrammatic representation of vascular components of glioblastomas.

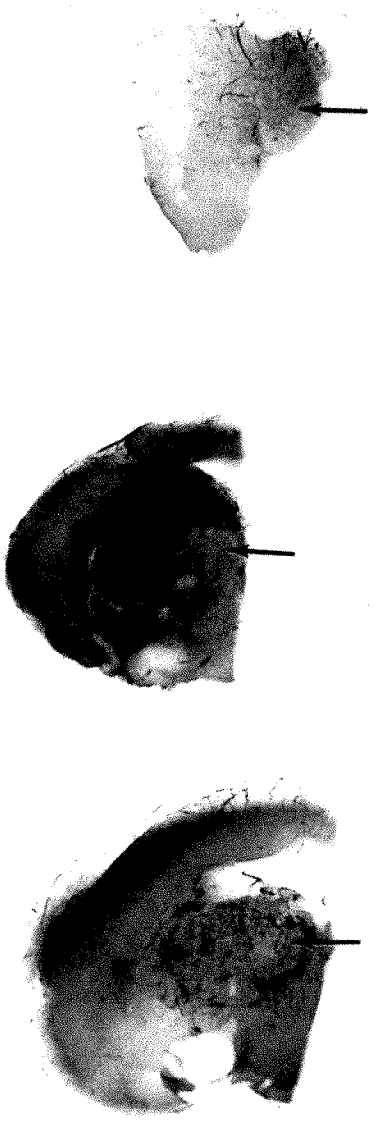


FIG. 11. Two millimeter coronal sections of guinea pig brain with transplanted human glioblastoma. Arrows denote lesion and irregular network of tumor vessels which have developed.

relatively large transcerebral and cortical arteries and veins which may undergo dilatation and deformation, presenting a coarse tumor vascularity in arteriograms.

A homogeneous blush seen in some glioblastomas would appear to be due to gray matter vasodilatation, as well as new vessel formation from gray matter arteries and veins invoked by tumor infiltration. A similar contrast material stain produced by gray matter vascularity can be seen in metastatic deposits, infarcts, and possibly in association with abscess formation. It is speculated that the richer vascular bed found in gray matter when involved by tumor may contribute to the more rapid growth of the glioblastoma.

A second major type of vascularity in glioblastomas is due to new vessel formation. The vessels which are primarily capillary in type may have an irregular formation without definite patterns or assume a spherical network configuration around necrotic or within viable tumor.

Brief comment is made concerning a guinea pig glioblastoma tumor model, which is now under investigation. Hopefully, postmortem vascular injections of these tumors at various stages of growth will give a clearer understanding of the development of glioblastoma vessels.

J. H. Scatliff, M.D.
Department of Radiology
University of North Carolina
School of Medicine
Chapel Hill, North Carolina 27514

The authors wish to acknowledge the help of Dr. Martin R. Krigman of the Department of Pathology, University of North Carolina School of Medicine, for his help in the analysis of the histologic material and generous aid in beginning a study of glioblastoma vascularity in guinea pig transplants.

The tumor material presented in this paper was collected at the St. George's Hospital, London (Atkinson Morley's Unit) England, and the West Haven, Connecticut, Veterans Administration Hospital.

REFERENCES

1. Davidoff, L. M. Some random thoughts on astrocytomas. *Bull. New York Acad. Med.*, 1966, *42*, 85–99.
2. Hardman, J. Angioarchitecture of gliomata. *Brain*, 1940, *63*, 91–118.
3. Heinz, E. R., and Cooper, R. D. Several early angiographic findings in brain abscess includ-

ing "the ripple sign." *Radiology*, 1968, *90*, 735–739.

4. Huang, Y. P., and Wolf, B. S. Veins of white matter of cerebral hemispheres (medullary veins): diagnostic importance in carotid angiography. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1964, *92*, 739–755.
5. Ide, A. G., Baker, N. H., and Warren, S. L. Vascularization of Brown-Pearce rabbit epithelioma transplant as seen in transparent ear chamber. Am. J. Roentgenol. & Rad. Therapy, 1939, *42*, 891–899.
6. Kernohan, J. W., Mabon, R. F., Svien, H. J., and Adson, A. W. Simplified classification of gliomas. *Proc. Staff Meet. Mayo Clin.*, 1949, *24*, 71–75.
7. Lassen, N. A. Luxury-perfusion syndrome and its possible relation to acute metabolic acidosis localised within brain. *Lancet*, 1966, *2*, 1113–1115.
8. Liliequist, B. Capillary phase in cerebral angiography. *Acta radiol.* (Diag.), 1967, *6*, 113–125.
9. Lindgren, A. G. H. Vascular supply of tumors with special reference to capillary angioarchitecture. *Acta path. et microbiol. scandinav.*, 1945, *22*, 493–522.
10. Lorenz, R. Differential diagnosis of arteriographic appearance of intracranial tumors: glioblastomas, meningiomas, sarcomas. *Zentralbl. Neurochir.*, 1940, *5*, 30–60.
11. Nyström, S. Pathological changes in blood vessels of human glioblastoma multiforme; comparative studies using plastic casting angiography, light microscopy and electron microscopy, and with reference to some other brain tumours. *Acta path. et microbiol. scandinav.*, 1960, Suppl. 137.
12. Robinson, F., Porro, R. S., and Scatliff, J. H. Angiographic recognition of occipital lobe infarction. *Neurology*, 1966, *16*, 1016–1021.
13. Scatliff, J. H., Crompton, M. R., and Bull, J. W. D. Post mortem brain tumor angiography. *Acta radiol.* (Diag.), 1966, *4*, 476–487.
14. Taveras, J., and Wood, E. H. Diagnostic Neuroradiology. Williams & Wilkins Company, Baltimore, 1964.
15. Wickbom, I. Angiographic determination of tumor pathology. *Acta radiol.*, 1953, *40*, 529–546.

THE BASIS FOR SEGMENTAL SEQUENTIAL IRRADIATION IN HODGKIN'S DISEASE: EXTENDED *VS.* LOCAL FIELDS IN THE RADIOCURABILITY OF THE SJL/J MOUSE HODGKIN'S-LIKE RETICULUM CELL SARCOMA*

By PHILIP RUBIN† *and* GLENN HALUSKA *with the Technical Assistance of* George Miller
ROCHESTER, NEW YORK

THE feasibility of protocol clinical investigation to establish a statistical and significant advantage for one method of treatment *versus* another is a function of the margin of superiority and availability of patients. In Hodgkin's disease, the current interest is high with regard to the issue of extended *versus* localized radiation fields to assure the highest survival rates in the early stage of the disease. Computations[9] from previous studies indicate that 472 cases would be required in Stage I disease to show an improvement of survival from a 68 per cent 5 year figure to 80 per cent. For Stage II disease, estimates of current survival rates of 40 per cent to be improved to 55 per cent would require 390 new cases to be studied. A period of 5 years would elapse to collect the required number of patients and another minimum of 5 years to obtain a valid answer. A properly designed study may require almost 1,000 new patients and a 10 year period before an answer were forthcoming.

As an interim measure, a search for animal models to solve clinical problems is a reasonable alternative. The limitation of experimental animal systems rests in the difficulties of extrapolating such studies to man. Nevertheless, some insight to a clinical problem can be obtained which would be impossible to achieve in man. Interest in the SJL/J mouse model of a Hodgkin's like reticulum cell sarcoma[9] has led to the development of a model which can be asked pertinent clinical questions. This study is a progress report detailing the patterns of spread, patterns of recurrence and response to radiation therapy.

PREVIOUS STUDIES

The "experimental model" to explore the spread and treatment of Hodgkin's disease was designed to have the following characteristics:[9]

(1) *Unicentric origin* of a lymphoma was essential.
(2) *Transplantable* lymphoma so that adequate numbers of animals would be used.
(3) *Consistent disease pattern clinically* and high lethality.
(4) *Curability by radiation therapy* was possible.
(5) *A Hodgkin's-like lymphoma* was sought.

The system that met these criteria was a SJL/J strain of mice described initially by Murphy[6] at the Jackson Laboratory in Bar Harbor, Maine. This arose spontaneously in a Swiss Webster stock in which 91 per cent mortality (39 of 43) was due to a reticulum cell type of neoplasm. The anatomic distribution and histologic pattern were similar to the multicellular Type B reticulum cell neoplasm occurring in older mice of the C57L, other strains and their hybrids

* Presented at the Sixteenth Annual Meeting of the Association of University Radiologists, Columbus, Ohio, May 8–11, 1968.
† Chief and Professor, Division of Radiation Therapy and Radioisotopes, The University of Rochester School of Medicine and Dentistry, and Strong Memorial Hospital, Rochester, New York.
Supported in part by Clinical Radiation Research Center Grant CA-11051-01, Public Health Service, and Total Lymphatic Irradiation Grant IN-18J, American Cancer Society.

as described by Dunn.[2] The involvement was predominantly retroperitoneal and abdominal, including mesenteric, pancreatic, renal and lumbar lymph nodes, Peyer's patches, spleen and liver (Fig. 1, *A* and *B*). Disease was also found in the lung, mediastinum, thymus and cervical lymph nodes. The serially transplanted line described by Wanebo *et al.*[12] in the SJL/J strain is a widespread lymphoid tumor in which mesenteric lymph nodes are often the first involved; splenomegaly, diffuse hepatomegaly and very prominent Peyer's patches also occur. They described an abnormality in immunoglobulins manifested as a γ_1 and γ_2 paraproteinemia (89 per cent), often preceding the overt disease. There is no anemia and the white blood cell counts are not increased, although a lowering of lymphocytes is noted.

Of major importance are the histologic findings which vary not only in cellular detail but from mouse to mouse and even from tissue to tissue in the same mouse (Fig. 2, *A-C*). The main proliferative feature in most reports is that of the reticulum

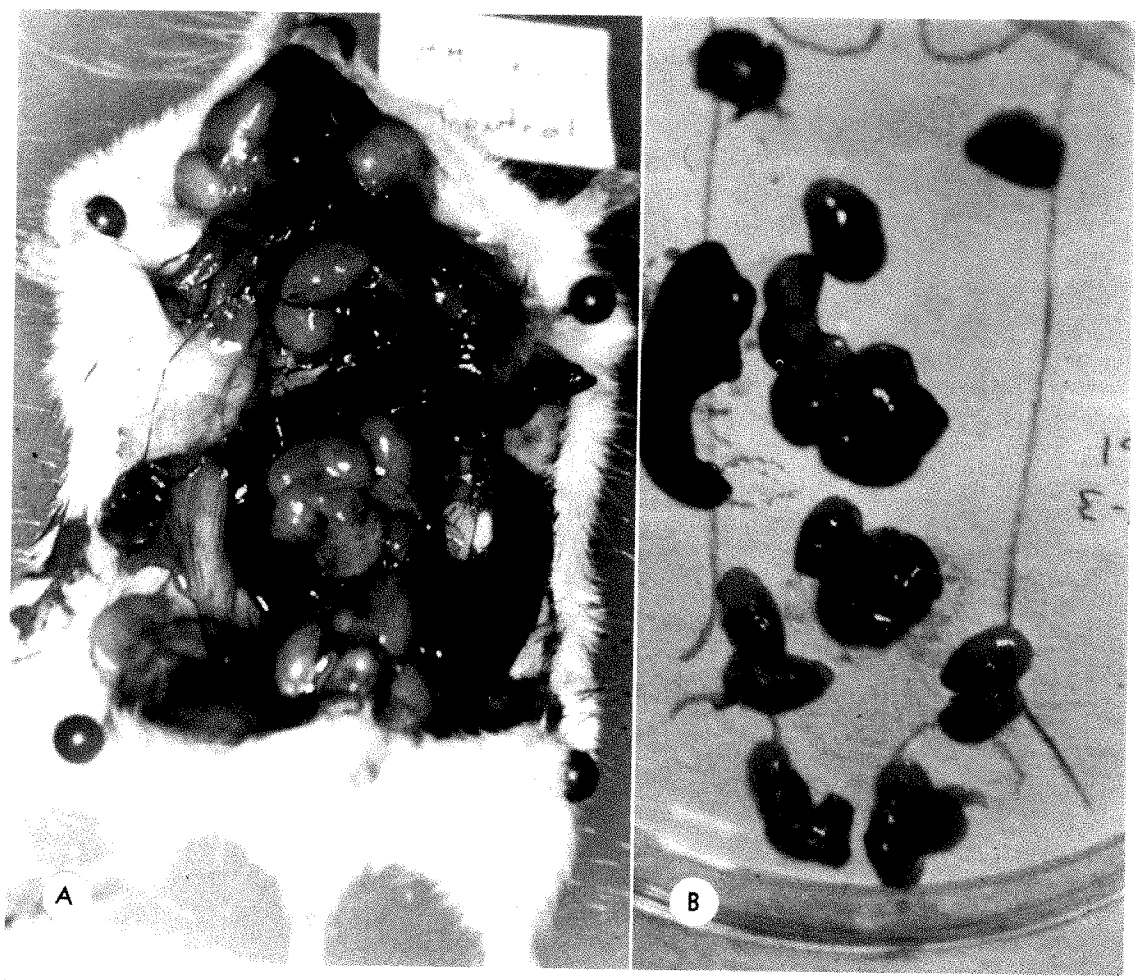


FIG. 1. The SJL/J mouse Hodgkin's-like reticulum cell sarcoma. (*A*) At postmortem examination in the end stages of the disease, the anatomic distribution of this lymphoma shows involvement predominantly of the cervical, axillary, mediastinal, retroperitoneal and inguinal lymph nodes. The enlarged spleen is characteristic and can be diffusely speckled or totally replaced. The liver is less consistently involved as are the Peyer's patches. (*B*) Distribution of enlarged lymph nodes after dissection is shown on the animal outline for easier identification. These lymph nodes vary from 1 to 2 cm. in size.

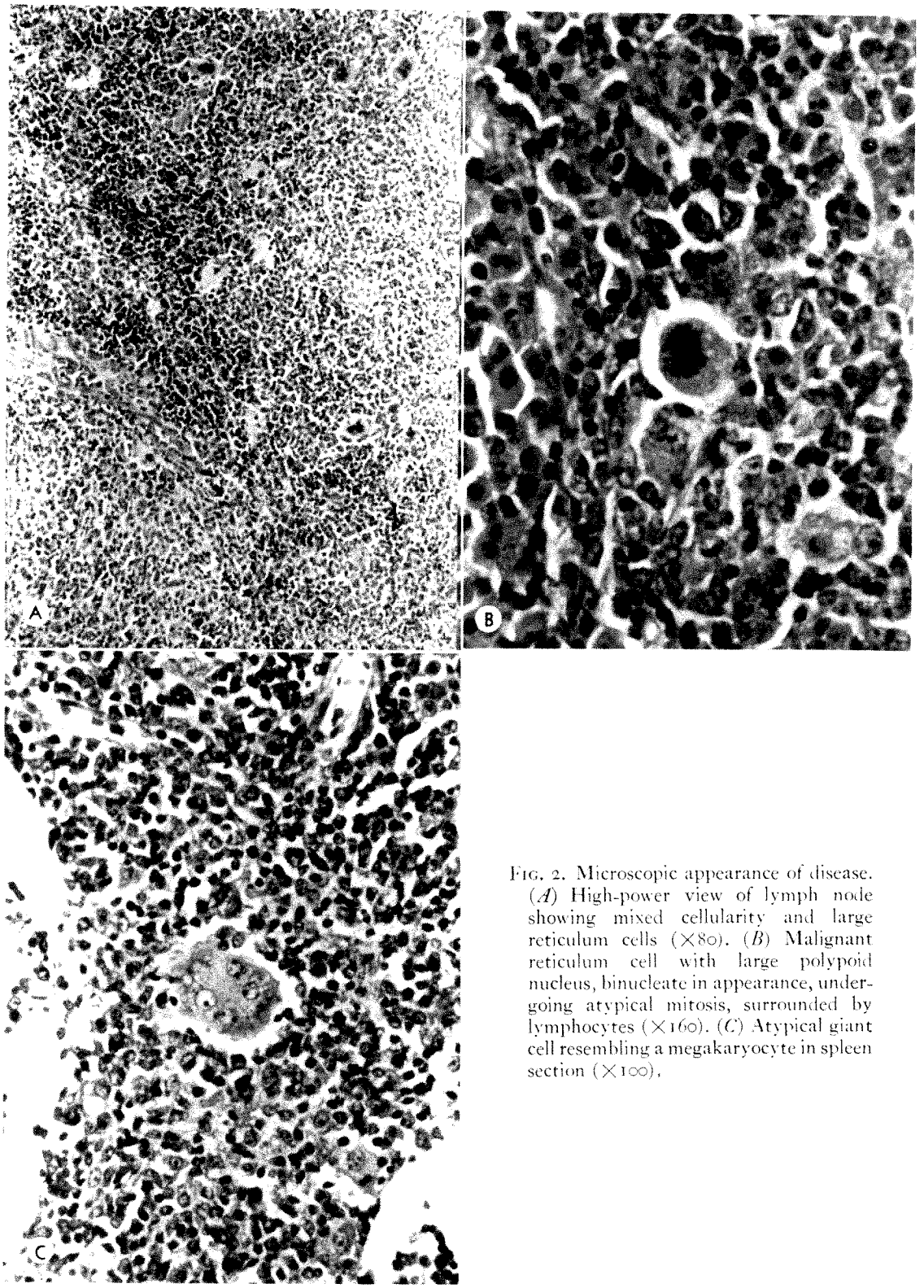


Fig. 2. Microscopic appearance of disease. (*A*) High-power view of lymph node showing mixed cellularity and large reticulum cells (×80). (*B*) Malignant reticulum cell with large polypoid nucleus, binucleate in appearance, undergoing atypical mitosis, surrounded by lymphocytes (×160). (*C*) Atypical giant cell resembling a megakaryocyte in spleen section (×100).

cell; the similarity to Hodgkin's disease lies in the tumor giant cells and variety of cells involved in the response.[2] Murphy[6] refers to "a background of large pale reticulum cells intermixed with other cell types . . . The most difficult of all reticular neoplasms to differentiate because of a resemblance to chronic inflammation . . . reticulum cells, binucleate resembling the Reed-Sternberg cell." He further emphasized that the tumor giant cells also resemble Reed-Sternberg cells. Our pathologist, Terry,[11] feels that these giant cells are megakaryocytes, but Wanebo *et al.*[12] state, "atypical giant cells appear to be distinguishable from megakaryocytes and occur at sites where megakaryocytes are not normally found in the mouse." Lukes,[5] reviewing 3 selected sections from our colony, emphasized that he could not recognize "a cytologic change that resembles even in a vague way the polyploidism . . . in Reed-Sternberg cells and none of the huge inclusion-like nucleoli." Again he emphasized the reticular cell proliferation. The most prominent early feature, according to Wanebo *et al.*,[12] is a plasma cell proliferation which changes into a reticulum cell process.

Our preliminary report[9] dealt with the following problems of unicentric origin and pattern of spread. To start the disease in a unicentric fashion, a high concentrate of cells in a small volume of 0.1–0.2 cc. was injected into the subcutaneous tissues (Fig. 3*A*). The bolus was injected distal to an axillary or inguinal lymph node site so that the cells would preferably drain into the respective lymph node bearing region. Invariably, the first detectable lymph node was the draining lymph node. No subcutaneous mass appeared at the injection site. A period of 3–5 weeks was required for the disease to appear. If the animals were sacrificed at the time of first lymph node appearance, in 50 per cent the disease was localized at the time by gross pathologic observation, and in the other half it had spread to other sites in a random pattern of involvement. If 2 lymph node sites became involved, such as the axilla and neck, complete dissemination of the disease was invariably found at the postmortem inspection. The disease also appeared to be highly variable in its rate of progression and lethality, so that each study required its own control group. Each experiment was initiated with transplantation of the disease into 50 animals who were randomized into different groups depending on the form of radiation treatment. It was established that local control or regression of the disease was possible. Fractionated treatment had to be abandoned in favor of single dose treatment to avoid unduly traumatizing these fragile mice.

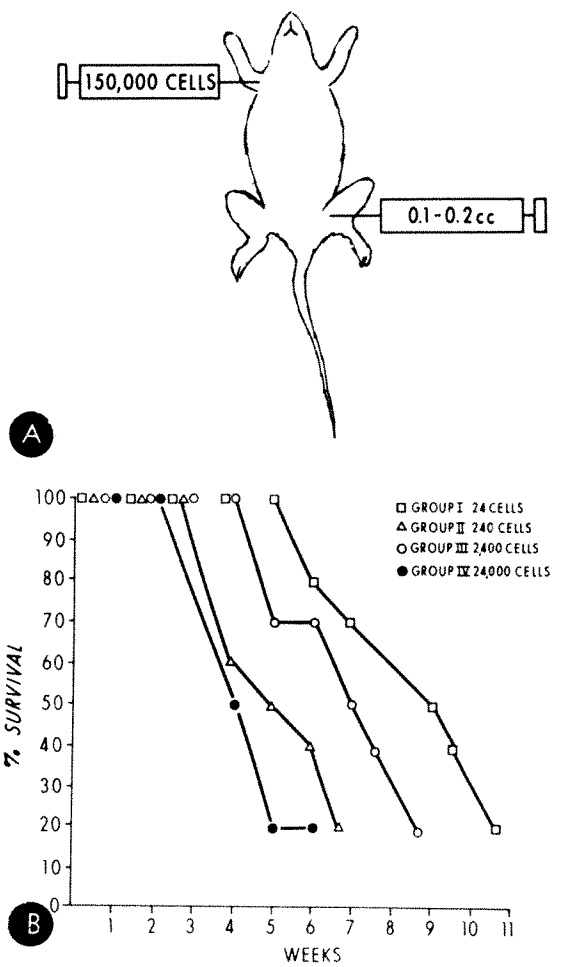


FIG. 3. (*A*) Experiment 1. SJL/J mouse lymphoma. Injection of a high concentrate of cells (150,000) in a small volume (0.1–0.2 cc.) distal to an axillary or inguinal lymph node site. (*B*) SJL/J mouse (HM 10). Number of cells related to induction time.

PRESENT STUDIES

This report deals with further studies to evaluate the basic problem: extended *versus* localized fields in curing lymphoma by radiation treatment. A number of experiments were undertaken to quantitate the transplantability characteristics of this tumor and to develop a more predictable rate of evaluation of the disease.

EXPERIMENT I: QUANTITATION OF INDUCTION

The early reports and experience with transplantation of this tumor suggested that large numbers of cells were required for a high take rate. Wanebo *et al.*[12] used 10 cells injected intraperitoneally and noted that a period of weeks was required for the disease to appear. Since the successful take rate was virtually 100 per cent in our laboratory, it seemed that subcutaneous inoculation was a better mode of administration. In studying 9 flights of 50 animals each, the number of cells inoculated was gradually reduced from 150,000 cells to 15,000 cells in a bolus to slow down the evaluation of the disease. To further establish the minimal number of cells required to induce the process, a direct attempt at calibration was made. A donor mouse was sacrificed, all the lymph nodes were dissected and then pulverized by nylon rotor in a test tube in a tissue culture medium (Hanks base medium 199). The lymph node mash was then strained through a fine mesh screen to eliminate the large clumps of cells. The cells were counted in a Coulter counter and hemocytometer, and serial dilutions were made. The difficulty in identifying the "tumor cell" in such a mixed population and establishing viability of cells is apparent. The injection bolus was kept to 0.1 to 0.2 cc. since larger volumes would ooze back through the needle track. Four groups were studied ranging from 24 to 24,000 cells.

Results. The induction time was directly related to the number of cells in the injection bolus (Fig. 3*B*). The rate of evaluation and lethality of the disease were the same. This indicates that once the cell line became established, the progression was unchanged.

EXPERIMENT II: DETERMINATION OF UNICENTRIC ORIGIN OF DISEASE BY LOCAL RADIATION THERAPY

The injection of the bolus locally cannot be equated with unicentric origin of a disease in a strict sense. Although the first overt manifestation was the local draining lymph node, it could be argued that, if microscopic study of all lymph nodes were undertaken, disease would be found. Indeed, the random pattern of spread noted in our preliminary study might be due to rapid dissemination of the cells by passing the local draining lymph node. The reason for the appearance of the disease first in the local draining lymph node could be a function of cell number rather than distribution. Before proceeding with the key study of extended radiation fields, it was important to demonstrate unequivocally that local field radiation could control the disease from spreading. The converse would follow: the disease was localized in the experimental design if local field irradiation could eradicate the disease.

A bolus of 12,000 cells in 0.1 cc. was injected into the right axilla under sterile conditions. Ten animals were studied in each of the following groups: pre-irradiation, immediately after injection, ½ hour to 1 hour, 1 day, and 1 week after injection, the time of the first lymph node appearance and a control group. The irradiation factors were: 200 kv., half-value layer of 1.00 mm. Cu, 1,500 r, through a field which encompassed the right axilla, neck and hemithorax, shielding the head and midline structures (Fig. 4*A*).

Results. (Fig. 4*B*). By local field irradiation, the disease never appeared overtly in the pre-irradiated group. Only 1 animal each in the immediate and 1 day group developed disease. The 1 week group developed some small inguinal lymph nodes and palpable spleen, but some of these minimal findings regressed and 60 per cent of these animals appeared to be controlled. The animals

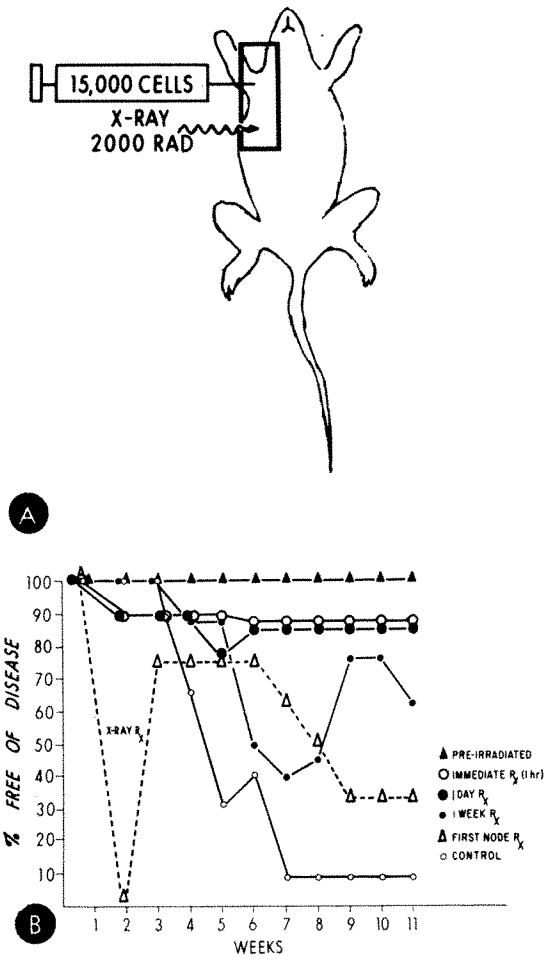


FIG. 4. (*A*) Experiment II. SJL/J mouse lymphoma. Unicentric origin. (*B*) SJL/J mouse (HM 14). Determination of unicentric origin of disease.

treated with the appearance of a definite lymph node showed regression of the local lymph node but disease appeared elsewhere showing control in only 30 per cent of the animals. The control group was a favorably selected slower onset group in which the disease appeared in all but 1 mouse by the eleventh week.

In conclusion, local field irradiation can control local disease in all mice and prevent the disease from spreading to other sites. The ability of irradiation to "cure" the animal is directly related to the time of treatment. Treatment in the subclinical induction time shows a high rate of curability. It is reasonable to postulate that the cells in the subcutaneous bolus are filtered by the draining lymph node. The ability to hold the disease is a function of cell number and probably cell biology and type. From past experiences with this model, we would expect that the escape of malignant cells from the lymph node would vary in repeated experiments because of cell type, but that cures are always possible with local irradiation. This substantiates the clinical postulate of unicentric origin of lymphomas by virtue of the observation that *local field irradiation can cure patients of their disease by eradication of localized disease.*

EXPERIMENT III: EFFECT OF EXTENDED FIELD IRRADIATION ON SURVIVAL

The induction of the disease was by axillary injection of a bolus of 15,000 cells in 0.1 cc. After a latent period of 2–3 weeks, the first lymph node appeared. The animals were randomized into 4 groups: control, hemithorax, thorax, and thorax-abdomen. The irradiation was carried-out with some shielding (Fig. 5*A*). There were 10 animals in each group. The treatment factors were: 200 kv., half-value layer of 1.0 mm. Cu, 1,000 r single dose.

Results. (Fig. 5*B*). The animals of the control group died of disease with striking adenopathy in all lymph node sites by the eleventh week. The best survival was obtained in irradiation above and below the diaphragm, with 80 per cent of the animals remaining free of disease. The 2 deaths were attributed to radiation injury since this scheme is at tolerance for these animals. Shielding of limbs, lungs and a portion of the liver was done. The slight advantage of total thorax fields (mantle) *versus* hemithorax (generous local field) is shown at 10 weeks (50 per cent *versus* 30 per cent) but is reduced at the 13th week (30 per cent *versus* 20 per cent). The attrition rate after the 13th week in the treated groups occurred sporadically and all animals autopsied remained free of disease. No obvious cause of death was consistently identified; spot blood cell counts did not reveal

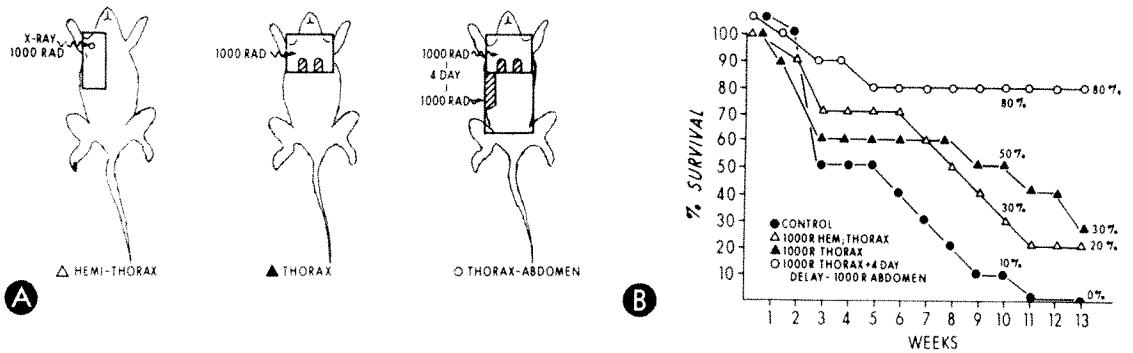


FIG. 5. (*A*) Experiment III. SJL/J mouse lymphoma. Effect of extended *vs.* local fields on survival. (*B*) SJL/J mouse (HM 11). Effect of extended fields on survival.

anemia, high white blood cell counts or abnormal cells on smear suggestive of a leukemoid or leukemic picture.

DISCUSSION: SPREAD, TREATMENT, RECURRENCE

The pattern of spread in lymphomas determines the logic of radiation treatment field arrangements. The evidence for unicentric origin of lymphomas has been developed clinically and in the SJL/J mouse model herein presented and rests on the postulate that *local field irradiation can cure patients (animals) of their disease by eradication of localized disease.* The argument for contiguous spread of Hodgkin's disease[8] is not the same as non-random spread (Fig. 6). If a lymph node site, such as the mediastinum, is surrounded by 4 other lymph node bearing regions, all of which can be involved with equal chance—the spread, although contiguous, is random.* This is even more apparent when lymph node bearing regions consist of 10–50 lymph nodes. Although this could be viewed as a semantic discussion, it has important clinical implications for deciding upon the best geometry for radiation treatment fields.

The escape of malignant cells of the lymphoreticular type from lymph nodes appears to be a function of cell number, cell proliferation and cell behavior. Prograde drainage into the next station of lymph nodes can occur in a non-random contiguous fashion. The probability of escape of malignant cells into the circulation and bypass of lymph nodes into larger lymphatic channels which drain into the blood stream increases as the number of lymph nodes involved increases. The importance of the post-capillary venules of lymph nodes as a site of re-entry into the circulation of lymphocytes has been shown by Gowans.[3,4] The detection of circulating Reed-Sternberg cells by Stofberg[10] and Bouroncle[1] is documented. The illusion of lymphatic spread of lymphomas may be due to recirculation and homing of lympho-reticular cells into lymph nodes and spleen.

CONCLUSION

The disparity between the clinical findings and the true pathologic extent of lymphomas as shown in our model is the rationale for extended field treatment. There is a higher recurrence or regional ex-

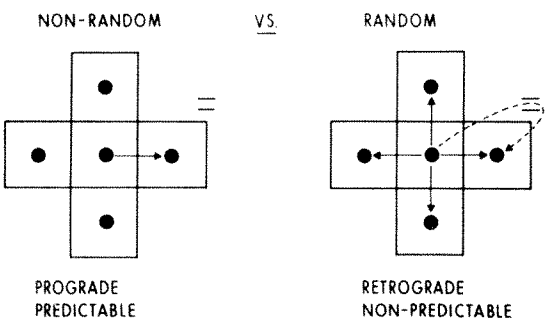


FIG. 6. Hodgkin's disease. Patterns of spread.

* Definition or statistics: Often characterizing a process of selection in which each item of a set has an equal probability of being chosen.

tension rate after treatment with localized fields than with extended fields in the early stage of the disease. The redistribution patterns following irradiation indicate that thorax bath or mantle techniques control the disease in the treated field but the abdominal recurrence rate in the mouse is high. The evidence after re-examining our clinical results with regard to recurrence patterns after mantle technique irradiation in Hodgkin's disease supports the observations seen in our animal model. The need to consider means of total lymphatic irradiation without injuring deep structures or increasing the radiation burden of potential long term survivors so as to shorten survival despite cure of the disease is a matter of vital concern. The future progress will be in the direction of re-exploration of segmental sequential irradiation of lymphoid tissue based on radiation pathology and functional changes in the lymphatic system.

Philip Rubin, M.D.
Division of Radiation Therapy
and Radioisotopes
The University of Rochester
School of Medicine and Dentistry and
Strong Memorial Hospital
Rochester, New York 14620

REFERENCES

1. Bouroncle, B. A. Sternberg-Reed cells in peripheral blood of patients with Hodgkin's disease. *Blood*, 1966, *27*, 544–556.
2. Dunn, T. B. Normal and pathologic anatomy of reticular tissue in laboratory mice, with classification and discussion of neoplasms. *J. Nat. Cancer Inst.*, 1954, *14*, 1281–1433.
3. Gowans, J. L. Recirculation of lymphocytes from blood to lymph in rat. *J. Physiol.*, 1959, *146*, 54–69.
4. Gowans, J. L., and Knight, E. J. Route of recirculation of lymphocytes in rat. *Proc. Roy. Soc., London*, 1964, *159*, 257–282.
5. Lukes, R. J. Personal communication, 1967.
6. Murphy, E. D. SJL/J, new inbred strain of mouse with high, early incidence of reticulum-cell neoplasms. *Proc. Am. Assoc. Cancer Res.* (Abst.), 1963, *4*, 46.
7. Nickson, J. J. Hodgkin's disease clinical trial. *Cancer Res.*, 1966, *26*, 1279–1283.
8. Rosenberg, S. A., and Kaplan, H. S. Evidence for an orderly progression in spread of Hodgkin's disease. *Cancer Res.*, 1966, *26*, 1225–1230.
9. Rubin, P. Hodgkin's-like reticulum cell sarcoma in SJL/J mouse: animal model of lymphoma to solve clinical problems. *Radiol. Clin. North America*, 1968, *6*, 25–40.
10. Stofberg, A. M. M. Significance of leukocyte concentrate in demonstration of tumour cells in blood. *Acta haemat.*, 1963, *29*, 65–79.
11. Terry, R. Personal communication, 1967.
12. Wanebo, H. J., Gallmeier, W. M., Boyse, E. A., and Old, L. J. Paraproteinemia and reticulum cell sarcoma in an inbred mouse strain. *Science*, 1966, *154*, 901–903.

THE BASIS FOR SEGMENTAL SEQUENTIAL IRRADIATION IN HODGKIN'S DISEASE: CLINICAL EXPERIENCE OF PATTERNS OF RECURRENCE*

By P. RUBIN,† G. HALUSKA *and* C. A. POULTER
ROCHESTER, NEW YORK

PATTERNS of recurrence in lymphomas provide us with further information as to their mode of spread. Following irradiation in localized forms of Hodgkin's disease, the initial site of reappearance of disease is a function of dose and field size. With the institution of more aggressive treatment in Hodgkin's disease, the first exacerbation of disease is no longer similar to that of a decade ago. The change in patterns of recurrence provides different reasons for treatment failure and offers new alternatives to therapeutic management. An evaluation of our clinical experience in 75 cases treated by the mantle field, and an experimental model of a Hodgkin's-like lymphoma indicate the value of segmental sequential irradiation of the total lymph node system (referred to from here on as SSI).

I. PROBLEMS OF CLASSIFICATION OF THE DISEASE

The attempt to arrive at a meaningful classification of disease classically follows two directions: anatomic staging of extent and histopathologic analysis. The major purposes of classification are to provide an index to prognosis and a guide to treatment. Although the evidence points to the increasing value of anatomic staging and correlating histologic types and staging, problems in practice exist.

The Peters classification[16] is a simple, clinical classification requiring careful examination, routine roentgenography and hematologic work-up. The dividing line between localized disease and advanced disease was whether the patient had 2 (Stage II) or 3 lymph node-bearing regions (Stage III) involved and whether the lymph node-bearing regions were contiguous or noncontiguous. Kaplan,[12] employing the information gained by lymphangiography, advocated the use of the diaphragm as a major dividing line between localized and more extensive disease, redefining Stage II and Stage III on the basis of disease above and below the diaphragm. The most recent alteration in staging has been advanced as an International Classification evolved at the Rye Conference (1966) and is currently the preferred system.[20] Stage I includes 1 or 2 contiguous lymph node-bearing regions, since the prognosis and survival figures are good or better in many series for the latter circumstance. Although it has not been publicized, the IUCC, using a TNM system, has a different variation on this theme.[10] These 3 systems are compared in a symbolic diagram and table which will be helpful to further discussion (Fig. 1; and Table 1).

The alteration in criteria for staging and the introduction of refinements in diagnosis render comparison with previous reports difficult. Since comparison of treatment methods rests upon identification of similar cases in different series, the improvement in results could be more apparent than real. The findings of Lee, Nelson and Schwarz[15] suggested that localized cases were indeed more disseminated and downstaging would

* Presented at the Sixteenth Annual Meeting of the Association of University Radiologists, Columbus, Ohio, May 8–11, 1968.
From Division of Radiation Therapy and Radioisotopes, The University of Rochester School of Medicine and Dentistry, and Strong Memorial Hospital, Rochester, New York.
This work was supported in part by Clinical Radiation Research Center Grant #CA-11051-01, NIH Public Health Service, and Total Lymphatic Irradiation Grant #IN-18J, American Cancer Society.
† Chief and Professor of Radiology.

follow, *i.e.*, conversion of approximately 40 per cent Stage I and II patients to Stage III. An analogy to cervical cancer could be made where apparent improvements in survival could be due to method of staging. If a patient is not given the benefit of doubt, Stage I patients can be downstaged into Stage II and lead to better results in both Stages with no real over-all improvement. One could argue that the current Stage I and II Hodgkin's disease patients have a truly localized process by virtue of current diagnostic techniques, and that the improvements in survival figures are due to selection, not therapeutic advances. Downstaging has *not* occurred in our experience (Fig. 2).

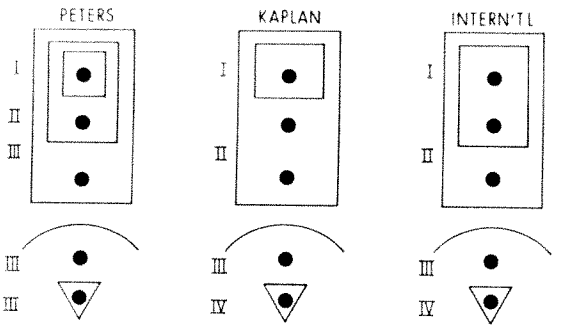


FIG. 1. Problems of classification. Using the form of symbolic staging, each lymph node-bearing region is represented as one black circle. Each box represents the stage as described in the accompanying table for each of the various classifications which have been generally accepted during the past decade. The curved line represents the diaphragm and the inverted triangle the visceral site. From this simple diagram, it can be readily appreciated the variation that exists in the different staging systems.

II. REDISTRIBUTION OF CASES

From Table II A, the redistribution of our cases can be appreciated, when patients are classified by the Peters, Kaplan and the International systems. Surprisingly, the major shift has not occurred in downstaging the disease but *upstaging*. That is, more of our cases have been included in the

TABLE I

HODGKIN'S DISEASE
DEFINITION OF STAGES

Stage	Peters	Kaplan	International
I	Involvement of single site or lymphatic region	Disease localized to single lymph node and contiguous structures without systemic symptoms	Disease limited to 1 anatomic region (I_1) or 2 contiguous anatomic regions (I_2) on same side of diaphragm
II	Involvement of 2 or 3 proximal lymphatic regions	Disease limited by the diaphragm to the upper or lower half of the body, more than a single side	Disease in more than 2 anatomic regions or in 2 noncontiguous regions on the same side of diaphragm
III	Involvement of 2 or more distant lymphatic regions	Disease above and below the diaphragm	Disease on both sides of the diaphragm but not extending beyond the involvement of lymph nodes, spleen, and/or Waldeyer's ring
IV	———	Disease demonstrated in any of the following areas: (1) bone marrow, (2) bone lesions, (3) pulmonary parenchymal lesions, (4) more than one cutaneous or subcutaneous lesion, (5) gastrointestinal tract, considered secondary	Involvement of bone marrow, lung parenchyma, pleura, liver, bone, skin, kidneys, gastrointestinal tract, or any tissue or organ in addition to lymph nodes, spleen, or Waldeyer's ring

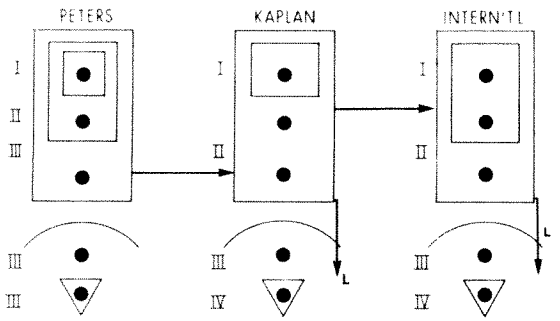


Fig. 2. Problems in classification. With variations in definitions of staging and the introduction of such sophisticated diagnostic techniques as lymphangiography, a redistribution of cases was bound to occur. The new definitions of Stage I show a definite trend toward upstaging, whereas lymphangiography would tend to downstage the disease. In our experience, upstaging has predominated over downstaging, as shown in Table II A.

Stage I group in the International classification than in the Peters classification. The major shift in cases between categories in the Peters and Kaplan classification has been to place more Stage III (Peters) into Stage II (Kaplan). The shift between the International and Kaplan classification has been to move Stage II (Kaplan) cases into Stage I (International). This has also been confirmed by our experience and the Walter Reed experience (Boyer *et al.*[2]) (Table II A and II B). The major factor in redistribution of cases has been one of redefinition of Stage I and II in the International classification, not lymphangiography.

III. The Role of Lymphangiography

Lymphangiography has been employed routinely since 1964. It has been performed successfully in 35 cases in this study and to date has slightly influenced the final staging of the patient. All studies in Stage I and II patients, except for one, were interpreted as negative or equivocally negative (Table III). Rather than discard Stage I and II patients without lymphangiography before 1964, all such patients have been classified as having negative lymphangiographic studies. The results of lymphangiography by Boyer *et al.*[2] in 100 consecutive

Table II A

Hodgkin's Disease
Redistribution of 75 Cases
(University of Rochester Medical Center)

Stage	Peters	Kaplan	International
I	16	15	43
II	27	48	20
III	32	3	3
IV	—	9	9

cases of early Hodgkin's disease patients indicate that only 6–10 per cent of cases were redistributed, and they question the value of this procedure in staging. The one positive lymphangiogram in our experience was in a patient with Stage II disease presenting with involved inguinal lymph nodes. Retroperitoneal disease would be expected in this instance. The other positive studies were in very advanced disease with palpable abdominal lymphadenopathy, Stage III by clinical examination.

The promise of lymphangiography in detecting subclinical disease on the other side of the diaphragm has not been fulfilled, based on our experience in Hodgkin's disease.

The most unexpected finding was the development of retroperitoneal nodal involvement in 15 patients with previously read negative lymphangiograms (Fig. 3). The appearance of disease below the diaphragm has been found in 1 of the equivocal lymphangiogram cases. A review of the lymphangiograms by one of our diagnostic radiologists (George Drake) has

Table II B

Hodgkin's Disease
Redistribution of 71 Cases
Walter Reed Experience[2]

Stage	Peters	Kaplan	International
I	19	19	37
II	18	41	23
III	34	8	8
IV	—	3	3

TABLE III

HODGKIN'S DISEASE
LYMPHANGIOGRAMS

Stage	Total Patients	No. of Examinations	Negative	Equivocal	Positive	Later Positive
IA	15	5	5	0	0	2
IA	22	13	11	2	0	5
IIA	13	8	5	2	1	6
I, IIB	13	5	4	1	0	3
III	11	4	0	0	4	0
	74	35	25	5	5	16

not resulted in reinterpretation of a study previously negative or equivocal to a positive status.

The inability of lymphangiography to detect microscopic disease has been alluded to in the report of Johnson and Cook.[11] Four cases of retroperitoneal lymphadenopathy developed in screened cases with positive supradiaphragmatic lymph nodes on presentation. Follow-up roentgenograms were of limited value since contrast media eluted from 5–12 months, and most media cleared in 2 years. A few residual flecks of contrast medium in strategic locations can establish growing disease, but in our experience a repeat study is indicated and was successfully achieved in virtually all of our cases.

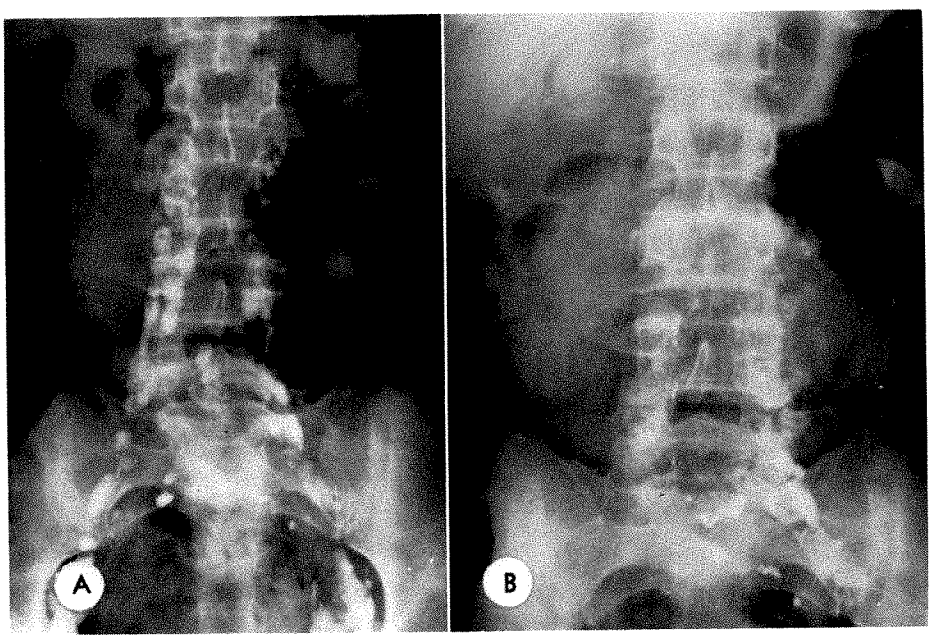


FIG. 3. Conversion of negative lymphangiograms. This patient, a 27 year old white male, presented with an asymptomatic collection of enlarged lymph nodes of 3 months' duration in the right cervical region without other evidence of disease. All studies including (*A*) the lymphangiogram were negative. The mantle technique was utilized and a dose of 4,900 rads in 30 days was delivered to the right cervical region and a minimal dose of 3,500 rads to all of the other sites. (*B*) Systemic signs developed 16 months after treatment and at that time repeat lymphangiography showed extensive involvement of the retroperitoneal lymph nodes. Only the left side was examined.

IV. PATTERNS OF RECURRENCE BY STAGE

The patterns of recurrence are a function of the disease and treatment. The first recurrent manifestation differs with the Stage of the disease at presentation and varies with the dose and field size employed in the initial therapy. The following definitions of Kaplar[12] have been modified because of the use of extended fields in radical radiation therapy regimes.

True recurrence is defined as the reappearance of lymphadenopathy or other evidence of activity in a treated field as the first new manifestation of Hodgkin's disease after an initial course of radiotherapy. When low doses were used, the reason given for a true recurrence was that the dose applied was inadequate. With levels of 3,500 to 4,000 rads, true recurrence could be considered evidence for radioresistance or retrograde recurrence (re-seeding) which would signal spread from an untreated focus.

Marginal recurrence is defined as disease appearing at or adjacent to the margins of an adequately treated field limited to one side of the diaphragm. Although this would be indicative of inadequate appreciation of the local extent of disease when localized fields were used, this definition loses its original meaning as extended fields have been employed. When a mantle field, or inverted Y, is employed, those foci of disease reappearing on the same side of the diaphragm are referred to as marginal recurrences. These may be adjacent to uninvolved as well as involved lymph node-bearing regions, as long as these lymph node regions have been treated.

Extensions are defined as new manifestations of disease in nonadjacent previously untreated areas. These extensions reflect the limitation of the diagnostic methods used to establish the initial clinical extent of disease. With the use of the mantle field or inverted Y field, extensions are applied to disease appearing for the first time on the other side of the diaphragm. Thus, retroperitoneal lymph node involvement as the first appearance of disease despite a previously treated positive mediastinum is classified as an extension, not as a marginal recurrence.

Dissemination is defined as invasion of viscera such as bone marrow, liver, lung, spinal cord, bone, etc. This would be indicative of spread beyond the lymph node system. Evidence for widespread disease will also be referred to as generalized disease. It should be evident that with the use of segmental sequential irradiation above and below the diaphragm, the terms true recurrence, marginal recurrence and extension will need redefinition again.

The reasons for reappearance of disease are more easily analyzed by Stage. The information is presented in a composite diagram (Fig. 4; and Table IV). For discussion, the International staging will be utilized and the corresponding Peters and Kaplan categories indicated in parentheses.

A. STAGE I_1 (STAGE IA PETERS; STAGE IA KAPLAN): 15 Patients

1. *Distribution.* The majority of patients presented with positive neck lymph nodes (9), more on the left than on the right side (6 *vs.* 3). Mediastinal, axillary and inguinal lymph node involvement was less common.

2. *Lymphangiography.* Five of the patients had lymphangiography and all were negative. Two of the five later developed dissemination to the retroperitoneal lymph nodes as the first reappearance of the disease. Four other patients without initial lymphangiographies were studied later when the disease was clinically disseminated and were positive.

3. *Reasons for failure.* The initial reappearance of disease in 6 cases was predominantly in the retroperitoneal area.

(a) True recurrence. There was 1 case of axillary lymph node recurrence in an adequately treated area (3,600 rads) which was attributed to reseeding, since involved retroperitoneal lymph nodes were detected simultaneously. There was 1 instance of an "in field" neck recurrence at

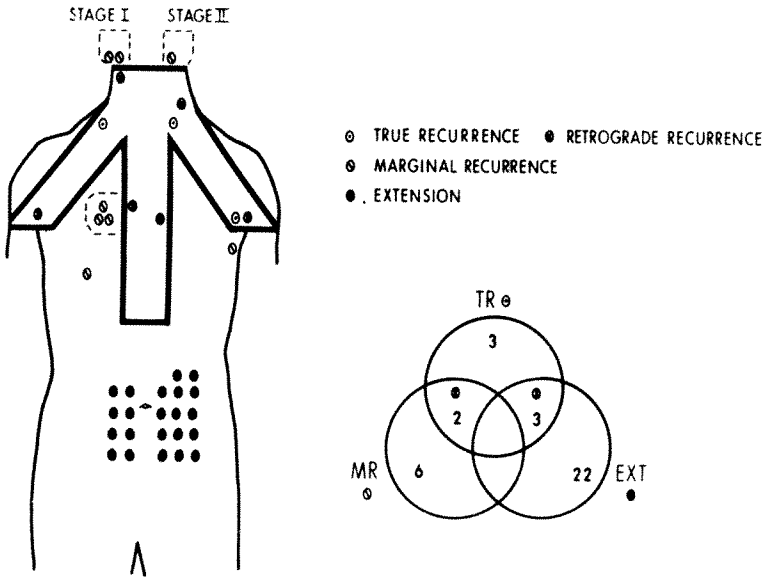


FIG. 4. Patterns of recurrence. This composite diagram indicates the first manifestation of disease in 65 patients followed a year and a half after the use of the mantle field therapy which is clearly indicated. The recurrences in Stage I patients are presented on the left hand side of the diagram and in Stage II patients on the right hand side. A Venn diagram to the right illustrates the overlapping recurrence patterns which are further elaborated in Table IV. It is quite clear from the Figure that extension below the diaphragm has been the predominant pattern of recurrence following the use of the mantle field.

an uninvolved site which was due to the low prophylactic doses used (2,000 rads).

(b) Marginal recurrence. There was a hilar recurrence in 1 patient who was estimated to have received less than 2,000 rads at the edge of a field.

(c) Extension. There were 4 cases of extension to the retroperitoneal lymph nodes of which 2 might have been excluded by lymphangiography, since they appeared within 6 months of the initial mantle treatment.

TABLE IV

HODGKIN'S DISEASE
PATTERNS OF RECURRENCE (FIRST MANIFESTATION)

Stage	No. of Patients	True Recurrence*	Marginal Recurrence	Extension	Dissemination	Recurrence Rate
I_1	15	1 (1)	1	4	0	6 (40%)
I_2	20	(2)	5	4	0	10 (50%)
IIA	12	2 (1)	2	6	1	11 (92%)
I, IIB	10	(1)	0	8	1	9 (90%)
III	8	(1)	0	3	5	8 (100%)
Total	65	3 (6) (5%)	8 (12%)	25 (39%)	7 (11%)	44 (69%)

* The number in parentheses indicates true recurrence associated with either a marginal recurrence or extension concurrently.

(d) Dissemination. There was no case of generalized disease or invasion of viscera as the first reappearance of disease.

(e) Subsequent recurrences. Two of the cases subsequently developed retroperitoneal lymph node involvement, 1 after local and 1 after marginal recurrence. No patient with recurrent disease is doing well or remains controlled at this time. Some were given chemotherapy, and others were treated below and/or retreated above the diaphragm to depth dose levels of 3,000 to 4,000 rads which were tolerated despite partial overlapping of previously treated fields.

Results. In summary, 6 of 15 patients developed exacerbation for a recurrence rate of 40 per cent.

B. STAGE I_2 (STAGE IIA PETERS; STAGE IIA KAPLAN): 22 Patients

1. *Distribution.* The majority of our patients treated were in this Stage. The mediastinum exceeded the neck as a site of involvement; the right neck was more commonly involved than the left neck, but the combination of involvement of the neck and mediastinum occurred in 77 per cent of all cases.

2. *Lymphangiography.* The majority of patients (13) had successful lymphangiographies. Of the 13 studies, only 2 were read as equivocally negative, but no redistribution in staging of cases occurred. Only 2 of the 13 cases developed later retroperitoneal lymph node involvement and these were not the equivocal readings.

3. *Reasons for failure.* The disease reappeared in 10 of the 20 patients (50 per cent) followed for more than 1 year and the pattern is different from the localized group in that marginal recurrence predominated as the initial event in 6 cases. Also, included in this group were 2 patients previously treated by surgical excision and watched and 2 treated by means of radiation therapy with small fields and inadequate doses.

(a) True recurrence. There were 2 local recurrences, 1 in the neck and 1 in the hilar area; but 1 appeared simultaneously with positive lymph nodes representing marginal recurrence, and the other later proved to be a retrograde reseeding problem from a retroperitoneal extension. Both were in sites which received 4,000 rads.

(b) Marginal recurrence. There were 5 marginal recurrences; 2 in the parotid gland region (Fig. 5*A*) and 3 in the hilar area (Fig. 5*B*). There was 1 large intrapulmonary nodal recurrence (Fig. 5*C*) which coalesced with the hilar lymph nodes.

(c) Extension. There were 4 instances of retroperitoneal lymph node involvement as the first new disease foci and 2 more on subsequent recurrences.

(d) Dissemination. None became generalized or showed invasion of viscera as the first sign, but 2 ultimately became generalized requiring chemotherapy.

4. *Results.* Four patients with marginal recurrence were successfully retreated with irradiation after doses of 4,000 rads. In these instances, overlapping fields were required totaling 8,000-9,000 rads surface doses which were well tolerated with minimal late sequelae. Two hilar and 2 parotid recurrences were thus controlled. Despite control of recurrences, 2 instances of eventual extension occurred. In 3 of the patients with extension below the diaphragm, vigorous radiation therapy was not employed and chemotherapy was used instead with failure to achieve control. The fourth has recently completed a radical course of radiation therapy below the diaphragm.

In summary, 9 of 22 patients (41 per cent) developed exacerbation of the disease.

C. STAGE IIA (STAGE IIIA PETERS; STAGE IIA KAPLAN): 13 Patients

1. *Distribution.* Of 13 patients with involvement of 3 sites, all but 1 above the diaphragm, the combination of mediastinal and bilateral neck involvement was the most common. The 1 patient with disease below the diaphragm had involvement of multiple lymph node sites including the spleen.

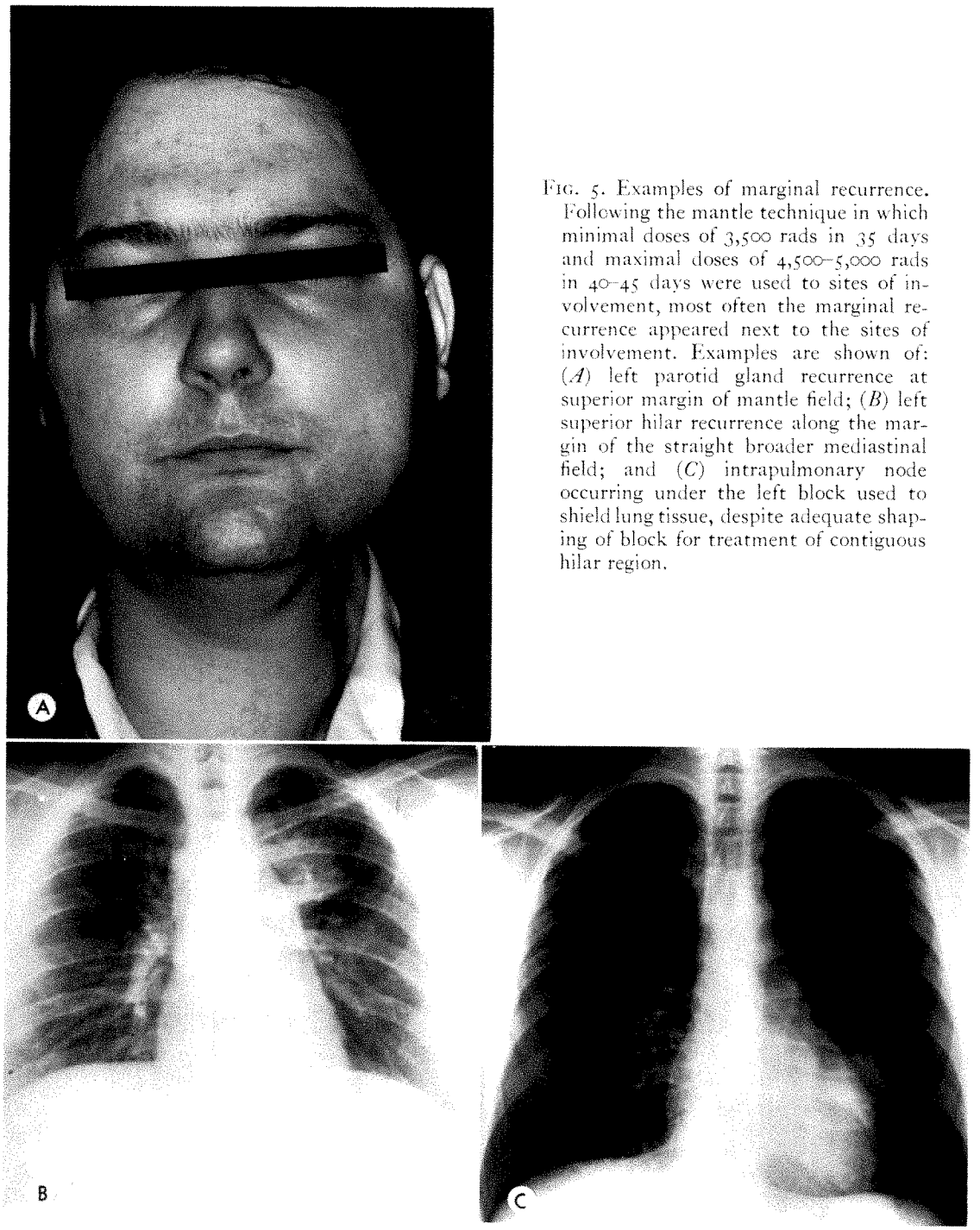


FIG. 5. Examples of marginal recurrence. Following the mantle technique in which minimal doses of 3,500 rads in 35 days and maximal doses of 4,500–5,000 rads in 40–45 days were used to sites of involvement, most often the marginal recurrence appeared next to the sites of involvement. Examples are shown of: (*A*) left parotid gland recurrence at superior margin of mantle field; (*B*) left superior hilar recurrence along the margin of the straight broader mediastinal field; and (*C*) intrapulmonary node occurring under the left block used to shield lung tissue, despite adequate shaping of block for treatment of contiguous hilar region.

2. *Lymphangiography.* The majority of patients had lymphangiographies (8 of 13) of which 5 were negative, 2 equivocally negative and 1 positive. The latter was in the patient presenting with involved inguinal lymph nodes. Again, no cases were redistributed on the basis of preliminary lymphangiography. The 1 equivocal case did develop positive retroperitoneal lymph nodes, but 4 others with retroperitoneal disease had negative studies.

3. *Reasons for failure.* The disease re-

appeared mainly as an extension below the diaphragm, but there were local and marginal recurrences also. Most foci of reactivation occurred within 2 years of the initial treatment.

(a) True recurrence. There were local recurrences in sites which received 4,000 rads (neck), 4,200 rads (neck), and 3,200 rads (axilla). There was 1 local recurrence concurrently with a retroperitoneal extension. Local recurrences on subsequent occasions were always associated with disease in other sites and were most likely reseeding problems.

(b) Marginal recurrence. There were 2 foci which fell into this category: 1 parotid and 1 subaxillary on the chest wall.

(c) Extension. Six patients developed retroperitoneal lymph node involvement, 1 with a true recurrence. Two developed disease in this site subsequently.

(d) Dissemination. One patient developed generalized disease as the first exacerbation.

(e) Subsequent recurrences. Most subsequent recurrences were paired—that is, combinations of local recurrence and retroperitoneal lymph node involvement appeared together or with marginal recurrences.

4. *Results.* Eleven of 12 patients developed new foci of disease—a recurrence rate of 92 per cent. Of these, 4 were retreated successfully: 1 had a marginal recurrence and 3 were cases of extension. The remaining 7 have not been controlled.

D. STAGES IIB (IIIB PETERS; IIB KAPLAN) BUT ALSO INCLUDES 3 CASES OF STAGE IB: 13 Patients

1. *Distribution.* The patterns of involvement were above the diaphragm with mediastinum, neck and axilla being involved with almost equal frequency. Most patients had mediastinal disease and 1 patient presented with involvement of lymph nodes below the diaphragm.

2. *Lymphangiography.* Five patients (above the diaphragm) were studied and all were negative except for 1 equivocal reading. One patient (below the diaphragm) was positive. No redistribution of cases in staging was made. Three patients with subsequent extensions had negative lymphangiograms initially.

3. *Reasons for failure.* All patients developed recurrence initially with disease first reappearing on the other side of the diaphragm. All reactivations occurred within the first year.

(a) True recurrence. There was 1 local recurrence, but this was associated with extension of disease.

(b) Marginal recurrence. No cases were found.

(c) Extension. Of the 8 recurrences, all were extensions into the retroperitoneal area indicating that a "B" designation means disease on the other side of the diaphragm.

(d) Dissemination. In 1 instance the disease became generalized. All subsequent exacerbations were generalized, requiring chemotherapy.

4. *Results.* Nine of 10 patients recurred for a 90 per cent failure rate. Only 1 case has reached 5 years without disease. Seven of the patients received treatment on the other side of the diaphragm and 1 has been controlled. All the others developed systemic involvement. The doses below the diaphragm were adequate (above 4,000 rads) in 4 instances, but inadequate in the 3 with lower doses of 1,800–2,700 rads.

E. STAGE IIIA, B OR STAGE IV (STAGE IIIA, B PETERS): 12 Patients

1. *Distribution.* The areas of involvement were ubiquitous with the disease being above and below the diaphragm clinically, or visceral disease being present. The neck was the most commonly involved site followed by the mediastinum, abdominal lymph nodes, retroperitoneal lymph nodes, and the spleen.

2. *Lymphangiography.* Of the 5 studies done, 4 were positive and 1 was equivocal. In many instances palpable disease was present.

3. *Reasons for failure.* Eight patients followed more than 1 year have failed to be

TABLE V

HODGKIN'S DISEASE
SURVIVAL FIGURES (1–7 yr.)

Stage	No. of Patients	Alive without Disease (per cent)	Alive with Disease (per cent)	Dead with Disease (per cent)	Dead with Intercurrent Disease (per cent)
I_1	15	60	13	27	0
I_2A	20	70	5	20	5
IIA	12	42	33	25	0
I, IIB	10	30	50	20	0
III	8	0	25	50	0

controlled thus far. The recurrence usually appears within the first year. It should be noted that this group includes many patients so toxic that only palliative therapy was done. Only those patients who did have a mantle field to high doses are reported in this study. No sites below the diaphragm were part of the initial radiation treatment plan, but chemotherapy was commonly used as part of the initial therapy.

(a) True recurrence. There was 1 local recurrence initially and that was associated with splenic involvement.

(b) Marginal recurrence. There was none.

(c) Extension. Three instances of retroperitoneal disease required eventual radiation. Consideration of this type of recurrence as an extension requires modification of the definition of "extension."

(d) Systemic involvement. Five patients developed systemic involvement as the first exacerbation and 1 subsequently.

(e) Subsequent recurrences. Virtually all areas became involved eventually.

4. *Results.* The main role of irradiation was palliative in this group. The recurrence rate has been 100 per cent. Irradiation above and eventually below the diaphragm followed in 6 cases and chemotherapy was used in 8.

F. SUMMARY OF RESULTS

Of the 74 cases treated by the mantle technique (or inverted Y), 64 are suitable for compilation of data with minimum follow-up of 1 year. The 8 patients presenting with extensions or dissemination are not included, since the disease cannot be encompassed by the technique of extended field irradiation limited to one side of the diaphragm. The 56 cases remaining were treated with the illusion that the treatment field encompassed all known disease, which was thought to be limited to one side of the diaphragm. Currently, 75 per cent are survivors with 1-7 years follow-up, of whom 54 per cent are free of disease and remain potential long term survivors (Table v). The patterns of recurrence suggest some deficiencies in our past radiation therapy techniques which are correctable. The recurrence rate averages 57 per cent but varies sharply between localized and contiguous disease (Stage I_1 and I_2) *versus* regionalized disease (Stage II) and systemic signs on presentation (B's); *i.e.*, 40 per cent *versus* 80 per cent. Cumulative survival curves for localized Stages I_1, I_2, IIA are shown in Figure 6*A* and indicate a rate of 75 to 86 per cent at 5 years. However, if those patients free of disease are noted separately, the best survival rate is seen for Stage I_2 at 63 per cent. Note the high persistence of disease in Stage II patients. The results achieved with Stage B patients with localized appearing disease (Stage I and II), as shown in Figure 6*B*, has been disappointing. Although Stage I and IIB survival rates are 67 per cent at 5 years, the recurrence free

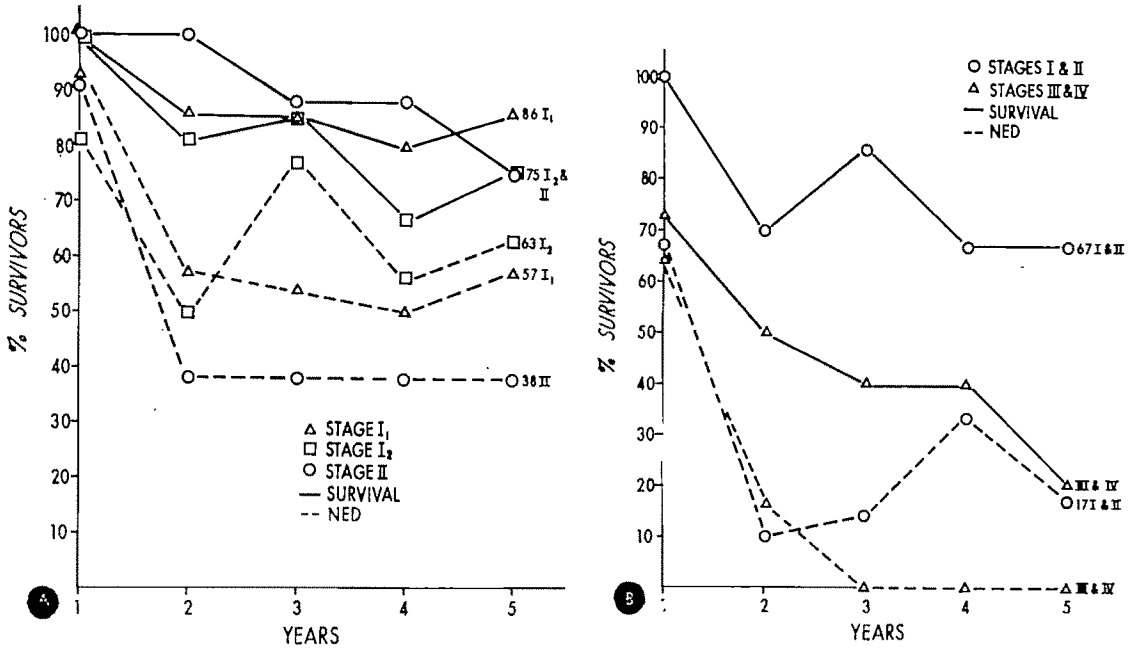


FIG. 6. (*A*) Survival pattern after mantle technique in Stage I_1, I_2 and II. (*B*) Survival pattern after mantle technique in Stage I, II, III, and IV.

survival is 17 per cent at 5 years.

(a) True recurrence (2 per cent, at most 12 per cent). The problem of true local recurrence has gradually been eliminated with radical treatment. Most authors have agreed to a minimum dose of 3,500 to 4,000 rads, respectively. The majority of true recurrences[7] were associated with disease outside the original treatment field, indicating that a reseeding mechanism could have been in effect. The argument, however, could be reversed but seems less likely. In either event, the local reappearance of disease in an adequately irradiated region should alert the clinician to disease elsewhere, particularly on the other side of the diaphragm.

(b) Marginal recurrence (18 per cent). There were 9 instances of marginal recurrence, rather evenly divided between parotid and hilar lymph node recurrences. There was 1 intrapulmonary node under the lung shields, but the others were failures of technique in the sense that larger shaped fields were required. Attention should be paid to inclusion of the hilar regions and the parotid gland area, the latter by a separate field if ipsilateral neck lymph node involvement is present. These two points should reduce the incidence of marginal recurrences.

(c) Extension (58 per cent). The major cause for treatment failure is extension to the other side of the diaphragm. As noted, lymphangiography has been relatively unsuccessful in our hands to detect microscopic or subclinical disease in the retroperitoneal region. In 11 cases of subsequent retroperitoneal involvement, suspicion of disease was raised in only 1 study, the others were all read as negative.

(d) Dissemination (2 per cent). In this group only 2 patients developed invasion of the viscera or bone marrow on initial presentation. In most cases generalization ultimately developed and required chemotherapy.

V. DISCUSSION

The original concept of segmental sequential irradiation (SSI) of major lymph node sites was introduced by Gilbert.[7] The

pursuit of such therapy was based on two observations: (1) the treatment of the overt clinical involvement failed because of marginal recurrences; and (2) the treatment of the entire trunk in sections because of the toxicity was carried out with low dosage and proved ineffective in controlling the disease.

This approach has been further explored by the Toronto group, and Peters[17] has carefully traced the evolution of techniques of "prophylactic" treatment of adjacent areas beyond the site of involvement in Hodgkin's disease. The balance between dose and field size seemed to be defined by Peters and Middlemiss[18] when an improvement in survival was recorded for higher doses to involved sites and lesser doses to uninvolved adjacent sites for localized cases. Five years later, two separate reports further polarized the search for the optimum plan of therapy into: (1) high dose therapy to local fields only (Easson and Russell[6]), *versus* (2) high dose therapy to extended fields (Kaplan[12]). The cycle has been completed with the recent report of Hynes[8] using the Gilbert technique of low dose therapy to extended fields with gratifying long term results.

A. HIGH DOSE THERAPY TO LOCAL FIELDS

The argument for this approach lay in the excellent results achieved by the Manchester group[4] with survival rates at 10 to 15 years which were comparable to those achieved by Peters.[17] Cure defined as recurrence free survival at 10 years was largely a function of dose, not extended fields, and prophylactic irradiation. The report of Peters[17] in which a skiagram considered both variables, dose level and prophylactic fields, supported the view of Easson and Russell.[5,6] The high dose to the site of involvement, not the larger fields, was the reason for success in radiation treatment in Peters' report.

B. HIGH DOSE TO EXTENDED FIELDS

The arguments for both high doses and extended fields were set forth by Kaplan.[12] Despite large doses to local fields, marginal recurrences were in evidence. In conjunction with Rosenberg[21] the orderly progression of spread from one site to adjacent sites was presented in an analysis of 100 consecutive cases. A prospective clinical study was organized utilizing localized *versus* extended fields. A progress report[1,19] has shown that localized fields for localized disease are yielding a similar survival pattern if supplemented by additional treatment to patients with recurrence. The recurrence rate is distinctly higher without use of extended fields. For Stage IIB and III patients, extending fields below the diaphragm has resulted in an improvement in control and survival. This is the first evidence based on controlled studies that prophylactic or extended fields may increase survival rates in Hodgkin's disease. It also reawakens interest in the technique of segmental sequential irradiation (SSI), since the extended fields used were field arrangements encompassing lymph node-bearing regions on both sides of the diaphragm.

C. LOW DOSE THERAPY TO EXTENDED FIELDS

The value of prophylactic treatment to extended fields with the use of low doses was suggested by Peters' skiagramatic analysis,[17] although not shown for high doses. For Stage I and IIA treated with low doses, a 25 per cent 5 year improvement was noted and at 10 years the only survivors (24 per cent) had extended fields treated. However, these results were not better than those achieved with high local dose treatment (44 per cent). Also, Hynes,[8] using the Gilbert technique, has a 10 year survival rate of 33 per cent in all comers with Hodgkin's disease. This is an isolated small series but compares favorably with Peters' best figure of 44 per cent at 10 years (high dose with extended field) and is distinctly superior to a 7 per cent 10 year figure (low dose with extended field) in all cases, *i.e.*, a combined average of 30 per cent.

D. SEGMENTAL SEQUENTIAL IRRADIATION

The technique of segmental sequential irradiation consists of irradiating all major lymph node regions in a fractional geometric manner. By concept, the technique means irradiation of lymph node-bearing regions in the upper segment defined by diaphragm and the lower segment (or *vice versa*) with exclusion of parts of vital organs by field arrangements and shaping. Total lymphatic tissue irradiation is impossible without total body irradiation. The use of shielding always means that some lymph node tissue is spared.

The feature to recognize when utilizing the technique of segmental sequential irradiation is that the delivery of doses of 3,500–4,000 rads to large volumes of tissue above and below the diaphragm is fraught with hazards. Even more than the mantle technique, such a program of radiation therapy in a potential long term survivor should only be undertaken by an experienced radiotherapist. There are numerous therapeutic possibilities in such a program and one has only to review the charted experience of Kaplan and Rosenberg[14] to appreciate the variety of approaches (Fig. 7, *A-E*).

1. *Sequential technique* is characterized by treating each segment to a desired total dose before proceeding to the next segment. This is usually done in a cephalad to caudad fashion. The mantle is commonly employed as the first part of treatment, followed by an interval of 1 month to treatment below the diaphragm. In our experience, if an inverted Y arrangement is used, severe depression of blood cell elements commonly occurs with platelet levels reading below 50,000 and white cell counts below 2,000. Interruption of treatment allows for recovery but prolongs time-dose relationship in the segment under therapy. At first this depression was thought to be due to splenic irradiation which was included with the inverted Y arrangement. This has not been completely substantiated in our new arrangement in which the spleen is treated alone and "in sandwich" between the mantle and inverted Y without an interval of rest (Fig. 7*C*).

The Stanford plan divides the abdominal and pelvic irradiation. The upper abdominal field includes the retroperitoneal lymph nodes and spleen but not liver, since radiation hepatitis can develop with doses of 3,500 rads to its entire volume. The ilioinguinal field follows in the sequence. Another approach is to treat the most involved segments first, abandoning a cephalad-caudad sequential coverage.

The important consideration in this

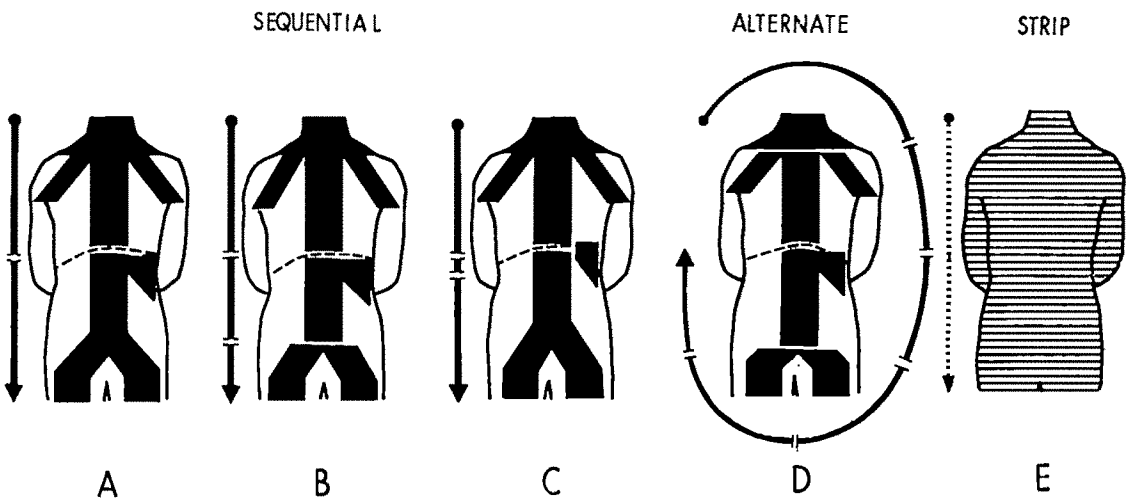


FIG. 7. Segmental irradiation. (*A–C*) Sequential. (*D*) Alternate. (*E*) Strip.

plan is the delivery of a specified dose in a specified time to a segment of involved lymph nodes. This usually is 3,500–4,500 rads in 3.5 to 4.5 weeks at the rate of 1,000 rads a week. The theoretic disadvantage of this technique is the potential of reseeding from an unirradiated focus of disease after treatment of the segment is completed. The therapeutic advantage may lie in the ability of normal lymphoreticular cells to repopulate the irradiated lymph nodes and the hope that the Reed-Sternberg cell does not reseed in the short resting time interval of 1 month.

2. *Alternate technique* is characterized by treating each segment to a modest dose until the entire cycle is completed. An interval of rest and repetition of the cycle follows. The dose-time schedules are abandoned in favor of a more rapid coverage of most lymph node sites. Doses of 200 to 1,500 rads can be delivered to the axillary, cervical, mediastinal, retroperitoneal, pelvic and inguinal fields as well as to the spleen. This can be repeated to raise the doses to higher levels up to 3,500–4,000 rads, but the time required to reach such levels in each specific volume could reach 90–120 days.

A rationale for this approach is to regard the Reed-Sternberg cell as similar to gonadal tissue with high radiosensitivity and low recovery capacity so that radiation injury is more cumulative than in other somatic tissues. Time may not be as critical as dose in Kaplan's review of the literature with regard to risk of recurrence in treated sites. Thus, *dose* not time-dose, is the cornerstone to the alternate field attack in segmental irradiation. The pathologic evidence in Hodgkin's disease, however, may call for a sequential approach, since these cells require larger doses and do not migrate rapidly or reseed irradiated sites. In lymphosarcoma, the alternate technique may prove more rewarding since the lethality of malignant lymphocytes can be achieved with smaller dose, and more rapid coverage of the anatomy may aid in catching up with the greater migrating capacity of the lymphocyte.

In conclusion, the technique of segmental irradiation using a sequential or alternate approach is a fertile area of investigation, not only in Hodgkin's disease but other lymphomas. Such variations as strip fields,[6] and extracorporeal irradiation[3] represent other forms of segmental or compartmental irradiation. The rationale for treatment will rest on a further understanding of the radiation pathology and physiology of the lymphatic system following irradiation of a lymphoid compartment (Fig. 8) or segment. The question of sensing or feed-

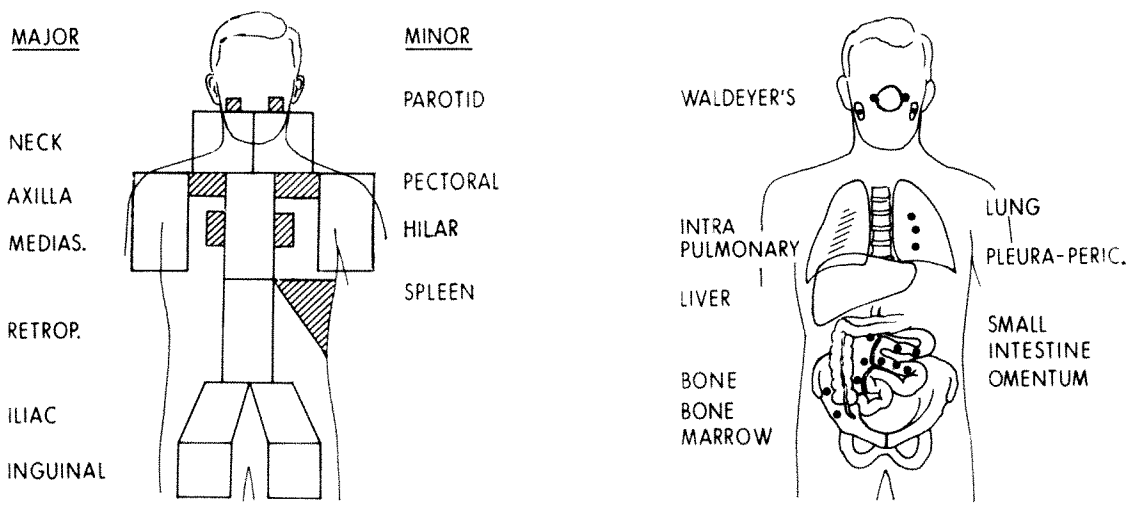


Fig. 8. Diagram of lymphoid compartments.

back between the depleted irradiated lymphoid segment (or compartment) and the nonirradiated segment remains to be answered. Is irradiation of a large segment *in vivo* capable of depleting all lymph nodes and producing an effective lymphopenia, as with extracorporeal irradiation? Does the irradiated depleted lymph node act as a magnet to attract migrating lymphocytes? If these hypotheses were correct, one could, in fact, be irradiating the total lymphatic tissue while fractionally irradiating one large segment.

RECOMMENDATIONS

1. Extended fields as the mantle (M) or apron fields (inverted Y) are advised for localized (Stage I_1) and contiguous disease (Stage I_2).

2. Segmental sequential irradiation (SSI) is advised for patients with involvement of 3 contiguous lymph node sites on one side of the diaphragm (Stage II), and all localized stages with systemic signs (Group B's) and lymph node disease above and below diaphragm (Stage III).

3. Local recurrence in adequately treated fields for localized or contiguous disease (Stage I_1 and Stage I_2) suggests a reseed mechanism and usually indicates that an extension is present. Local retreatment plus radiation therapy to the other side of the diaphragm will be required.

4. Chemotherapy is reserved for invasion of the liver, bone, bone marrow, lung, etc., or in the presence of systemic signs without overt or detectable lymph node involvement after extended field irradiation.

5. The argument for selection of some Stage I_1 and Stage I_2 patients for SSI may lie in histology. Cases of mixed cellularity and lymphocytic depletion can be considered candidates for such radical therapy.

Philip Rubin, M.D.
Division of Radiation Therapy
and Radioisotopes
The University of Rochester
School of Medicine and Dentistry and
Strong Memorial Hospital
Rochester, New York 14620

REFERENCES

1. BAGSHAW, M. A., KAPLAN, H. S., and ROSENBERG, S. A. Extended-field radiation therapy in Hodgkin's disease: progress report. *Radiol. Clin. North America*, 1968, *6*, 63–70.
2. BOYER, C. W., JR., BRICKNER, T. J., JR., and PERRY, R. H. Study of survival in 279 cases of Hodgkin's disease. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1968, *102*, 613–618.
3. CRONKITE, E. P., CHANANA, A. D., and SCHNAPPAUF, H. Extracorporeal irradiation of blood and lymph in animals: its effect on homografts and on lymphoma. *New England J. Med.*, 1965, *272*, 456–461.
4. EASSON, E. C. Long-term results of radical radiotherapy in Hodgkin's disease. *Cancer Res.*, 1965, *26*, 1244–1247.
5. EASSON, E. C., and RUSSELL, M. H. Cure of Hodgkin's disease. *Brit. M. J.*, 1963, *1*, 1704–1707.
6. FULLER, L. M. Lymphomatous disease. In: The Textbook of Radiotherapy. Edited by G. H. Fletcher. Lee & Febiger, Philadelphia, 1966, pp. 367–685.
7. GILBERT, R. Radiotherapy in Hodgkin's disease (malignant granulomatosis): anatomic and clinical foundations; governing principles; results. AM. J. ROENTGENOL. & RAD. THERAPY, 1939, *41*, 198–241.
8. HYNES, J. H. Curative treatment of Hodgkin's disease. To be published.
9. INGOLD, J. A., REED, G. B., KAPLAN, H. S., and BAGSHAW, M. A. Radiation hepatitis. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1965, *93*, 200–208.
10. IUCC Staging. Personal communication.
11. JOHNSON, R. E., and COOK, P. L. Hodgkin's disease: negative lymphogram in guiding radiotherapy. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1968, *102*, 883–890.
12. KAPLAN, H. S. Evidence for tumoricidal dose level in radiotherapy of Hodgkin's disease. *Cancer Res.*, 1966, *26*, 1221–1224.
13. KAPLAN, H. S. Radical radiotherapy of regionally localized Hodgkin's disease. *Radiology*, 1962, *78*, 553–561.
14. KAPLAN, H. S., and ROSENBERG, S. A. Extended-field radical radiotherapy in advanced Hodgkin's disease: short-term results of two randomized clinical trials. *Cancer Res.*, 1966, *26*, 1268–1276.
15. LEE, B. J., NELSON, J. H., and SCHWARZ, G. Evaluation of lymphangiography, inferior venacavography, and intravenous pyelography in clinical staging and management of Hodgkin's disease and lymphosarcoma. *New England J. Med.*, 1964, *271*, 327–337.
16. PETERS, M. V. Study of survivals in Hodgkin's

disease treated radiologically. Am. J. Roentgenol. & Rad. Therapy, 1950, *63*, 299–311.
17. Peters, M. V. Prophylactic treatment of adjacent areas in Hodgkin's disease. *Cancer Res.*, 1966, *26*, 1232–1243.
18. Peters M. V., and Middlemiss, K. C. H. Study of Hodgkin's disease treated by irradiation. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1958, *79*, 114–121.
19. Quie, P. G., Kaplan, E. L., Page, A. R., Gruskay, F. L., and Malawista, S. E. Defective polymorphonuclear-leukocyte function and chronic granulomatous disease in two female children. *New England J. Med.*, 1968, 278, 976–980.
20. Rosenberg, S. A. Report of Committee on Staging of Hodgkin's disease. *Cancer Res.*, 1966, *26*, 1310.
21. Rosenberg, S. A., and Kaplan, H. S. Evidence for orderly progression in spread of Hodgkin's disease. *Cancer Res.*, 1966, *26*, 1225–1231.
22. Shalek, R. J., Worsnop, R. W., and Sampiere, V. A. Radiation measurement and dosimetric practices. In: The Textbook of Radiotherapy. Edited by G. H. Fletcher. Lee & Febiger, Philadelphia, 1966, pp. 3–31.

VOL. 105, NO. 4

THE LAMINA DURA (L. D.) OF THE MAXILLARY ANTRUM: ITS VALUE IN ROENTGEN DIAGNOSIS*

By T. EL GAMMAL, M.B., CH.B., D.M.R., D.S., F.F.R., *and* THEODORE E. KEATS, M.D.
CHARLOTTESVILLE, VIRGINIA

FRACTURE or destruction of the posterior superior surface of the maxillary antrum cannot usually be demonstrated on routine plain roentgenograms of the sinuses. During the last year, we have included an additional special frontal view of the maxillary antra to our routine studies in order to investigate the paranasal sinuses. In this view the posterior superior surface of the maxillary antrum bordering the inferior orbital fissure appears as a continuous well defined thin line, the lamina dura (L. D.) (Fig. 1; and 2, *A* and *B*). The purpose of this report is to describe the technique for obtaining this projection and the type of information one may derive from it.

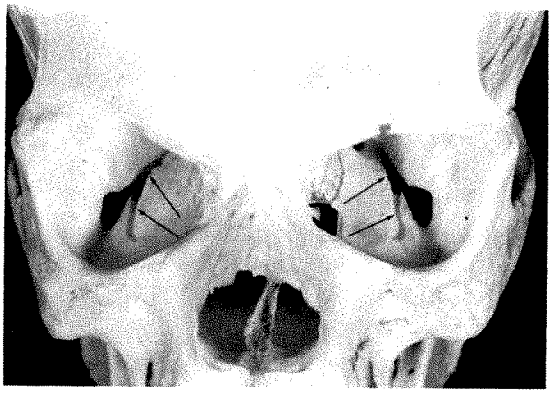


FIG. 1. Photograph of the skull showing the inferior orbital fissures. The medial border is formed by the posterior superior surface of the maxillary antrum, the lamina dura (L. D., upper arrows). Note the posterior openings and posterior parts of the infra-orbital canals (lower arrows).

TECHNIQUE

The patient is placed supine with the orbito-meatal line perpendicular to the cassette. The central roentgen ray is centered on the glabella, with the tube angulated 25° to the feet. A slit localized view of the L. D. is obtained. The recommended exposure is 80 kvp., 50–100 mas.

A similar view, to demonstrate the inferior orbital fissure, was used by Hartman and Gillies in 1959,[1] the so-called Blineau projection. In this projection, the patient is placed prone with the head flexed so that the plane of Virchow subtends a 20° angle with the vertical plane. The central ray is directed vertically and passes through the plane of the inferior orbital fissure. We believe that our projection made in the supine position is easier to obtain, particularly in an injured patient and demonstrates the lamina dura more clearly.

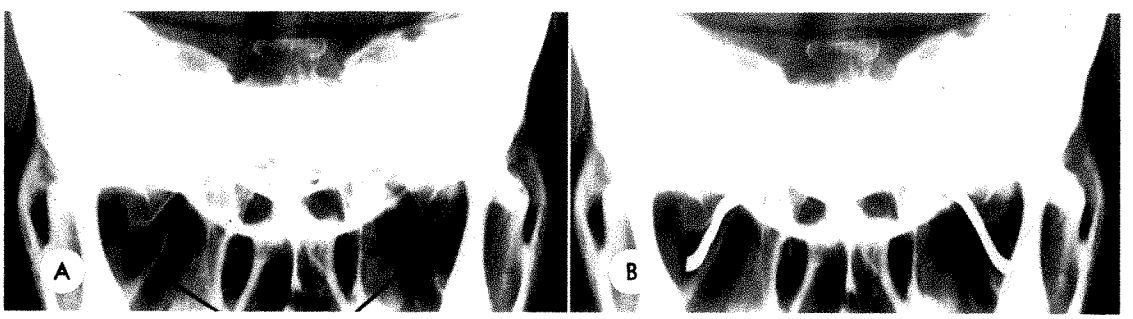


FIG. 2. L. D. view of the dry skull. (*A*) Both L. D. are seen as continuous dense lines. Note the posterior openings of the infra-orbital canals (arrows). (*B*) Same view with lead strips placed over the L. D.

* From the Department of Radiology, University of Virginia School of Medicine, Charlottesville, Virginia.

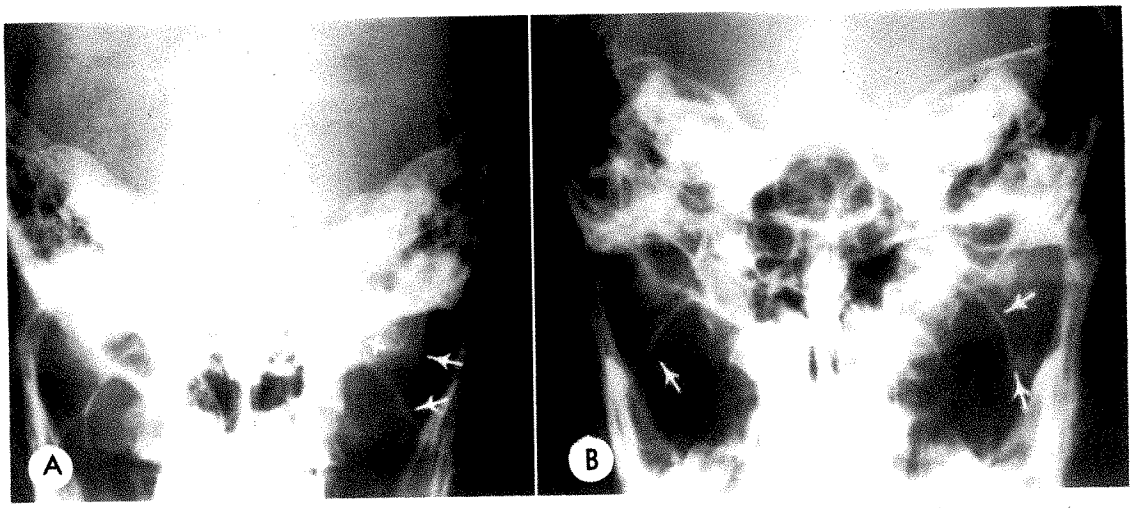


Fig. 3. Normal L. D. (*A*) Note the inferior orbital fissure (X), L. D. (lower arrow) and styloid process (upper arrow). (*B*) Another case of normal antra. Note L. D. (arrows) and the lateral end of the inferior orbital fissure (lower arrow on reader's right).

THE LAMINA DURA (L. D.)

The L. D. can be traced from about 2 cm. from the midline in the upper part of the roentgenogram, downwards (anatomically forward) and laterally as a dense continuous line. It is usually straight but may be wavy in its low (anterior) part. This appearance was seen in most normal cases (Fig. 3, *A* and *B*; and 4, *A* and *B*). Sometimes the posterior opening of the infraorbital canal, passing through the roof of the maxillary antrum, is shown as an indentation and should not be mistaken for a fracture (Fig. 2*A*). It is very important that the patient's head be straight because rotation will produce some asymmetry of the L. D. on both sides. The distance between the zygomatic arch and the neck of the mandible should be equal on both sides.

VALUE OF THE METHOD

The usefullness of this view is illustrated in several categories of disease.

Fractures. In facial fractures this view proved useful in demonstrating fractures which extend to involve the L. D. The L. D. may appear either interrupted (Fig.

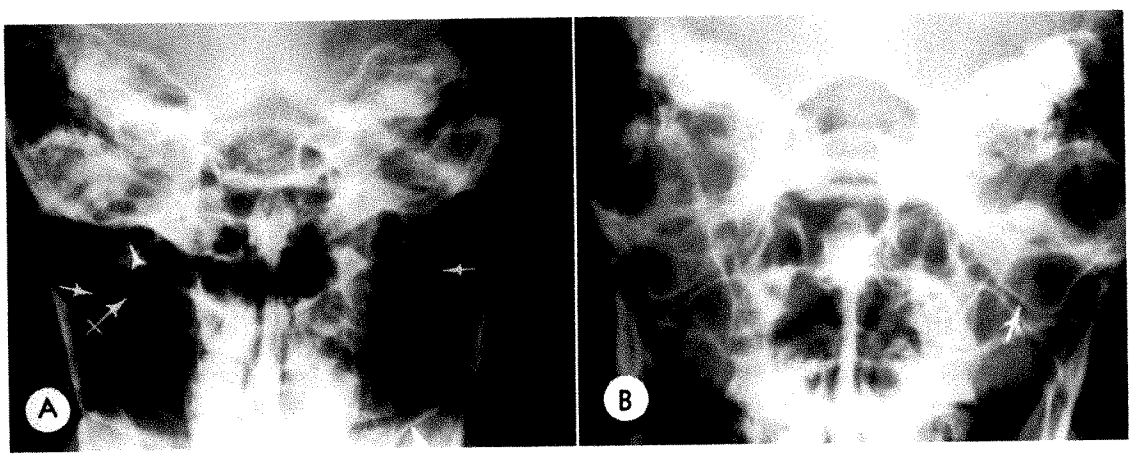


Fig. 4. (*A*) Note L. D. as continuous defined lines (→), right inferior orbital fissure (↔), and right styloid process (▲). (*B*) Well defined L. D. and left inferior orbital fissure (arrow).

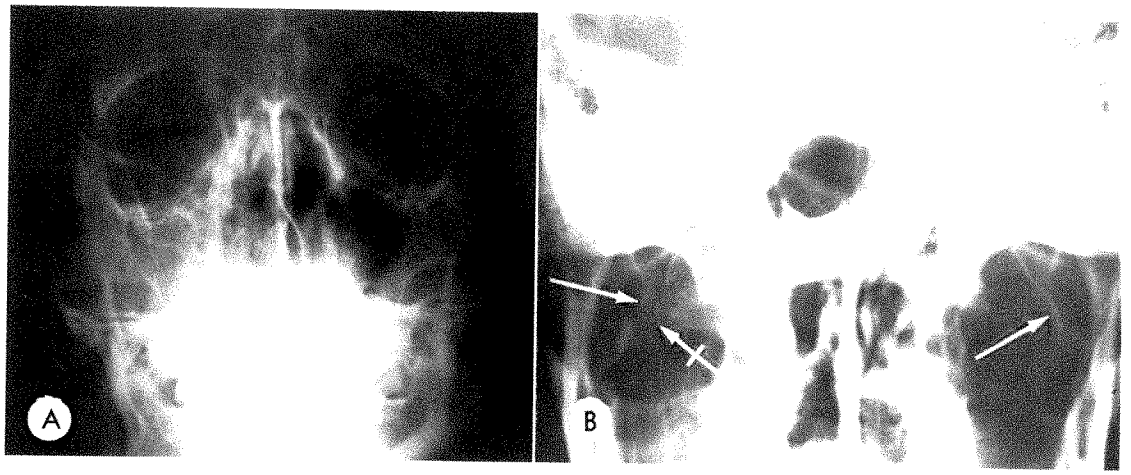


Fig. 5. Blow-out fracture of right antrum. (*A*) Waters' view shows opaque right antrum. (*B*) L. D. view reveals interruption of right L. D. (→), displaced piece of bone lying medially inside maxillary antrum (↔), and normal left L. D. (→).

5, *A* and *B*) or comminuted with spicules of bone displaced into the antrum (Fig. 6).

Neoplasms. Tumors involving the posterior-superior surface of the antrum will produce erosion of the L. D., best appreciated when compared with the contralateral side.

REPORT OF CASES

Case 1. Epidermoid carcinoma of right antrum. R. D., a 44 year old female, was admitted to the University of Virginia Hospital, July 5, 1967, complaining of painless swelling of the right cheek for 4 months. Prior to admission, this was treated conservatively with antibiotics, but the swelling continued to increase in size. The patient developed diplopia 2 months before admission. On examination, there was a 3×3 cm. firm fixed mass in the right lateral orbital rim with anesthesia along the second division of the trigeminal nerve. The Waters' view showed homogeneous opacity of the right antrum and

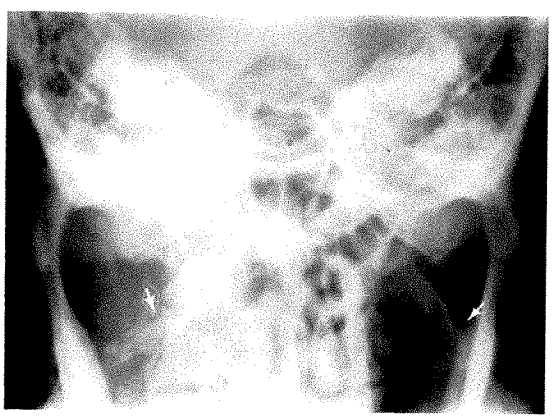


Fig. 6. Comminuted fracture of right antrum. L. D. view showing comminution of right L. D., bone spicules seen displaced medially inside the right antrum (arrow), and normal left L. D. (arrow).



Fig. 7. Case 1. Epidermoid carcinoma of right antrum. Waters' view shows opaque right antrum. No obvious bone destruction is seen.

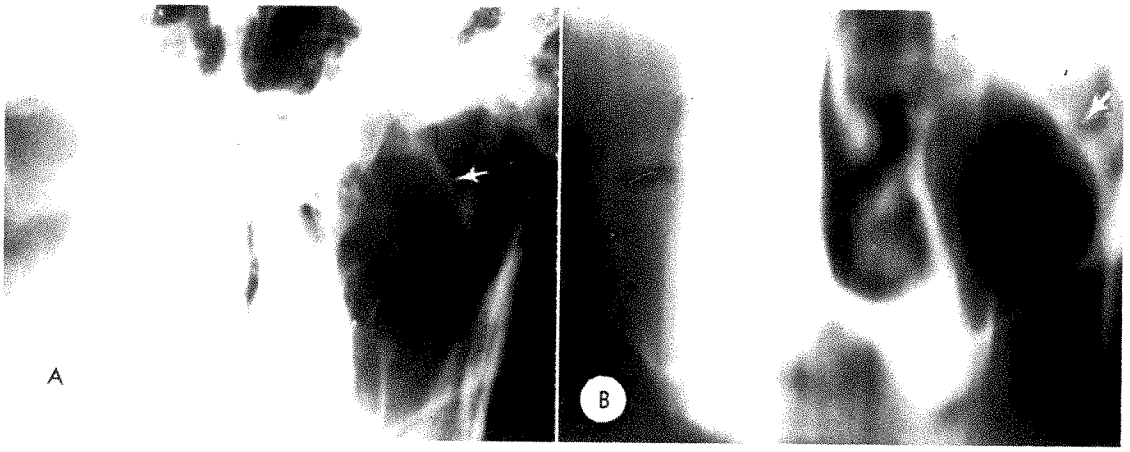


FIG. 8. Case I. Epidermoid carcinoma of right antrum. (*A*) L. D. view shows absent L. D. of the right opaque antrum, and normal left L. D. (arrow). (*B*) Tomogram reveals destruction of the posterior superior wall of the right antrum (arrow).

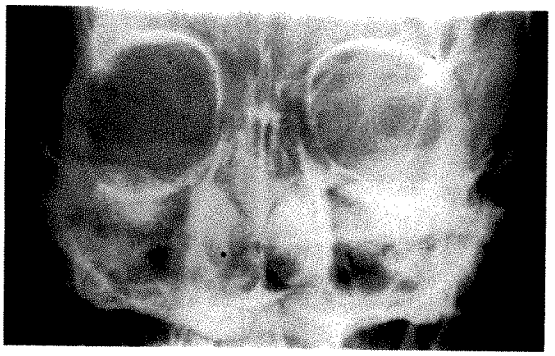


FIG. 9. Case II. Extensive meningioma of right middle fossa. Posteroanterior view with 25° angulation. There is marked destruction of both wings of the right sphenoid. The right ethmoid air cells are opaque.

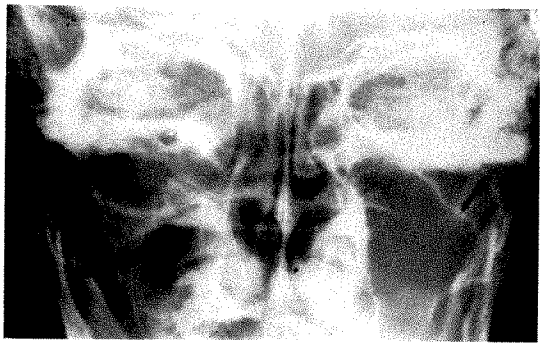


FIG. 10. Case II. L. D. view with 15° angulation. There is destruction of the right L. D. Note the normal left L. D. (arrow).

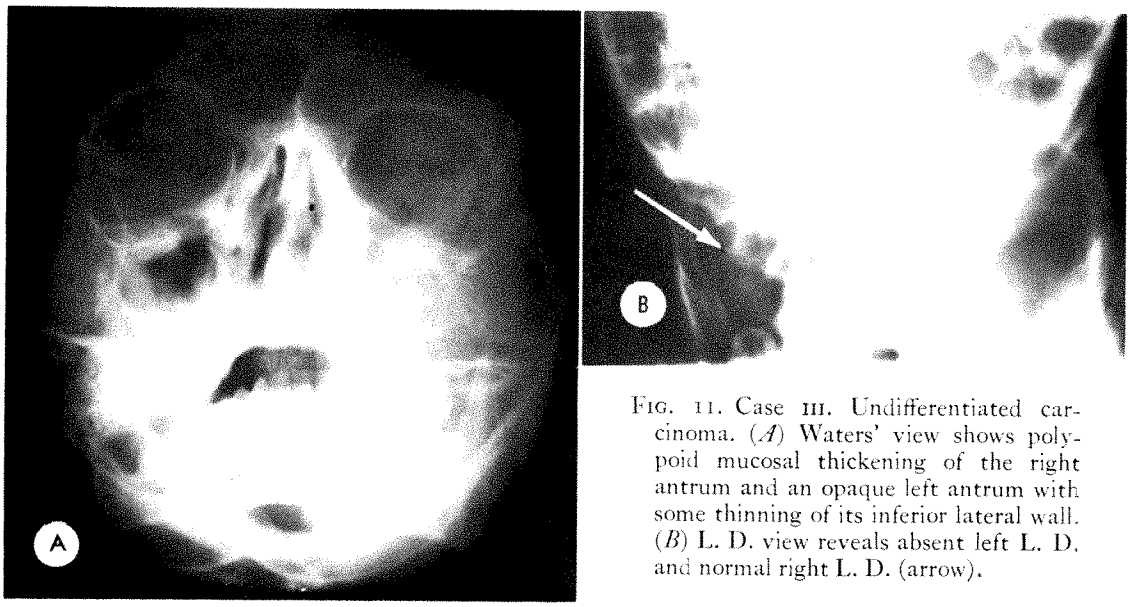


FIG. 11. Case III. Undifferentiated carcinoma. (*A*) Waters' view shows polypoid mucosal thickening of the right antrum and an opaque left antrum with some thinning of its inferior lateral wall. (*B*) L. D. view reveals absent left L. D. and normal right L. D. (arrow).

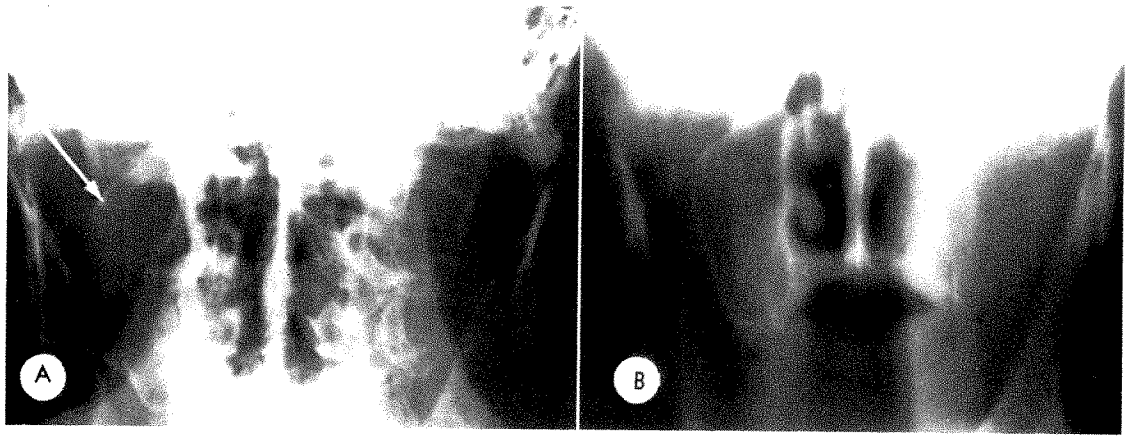


Fig. 12. Case IV. Reticulum cell sarcoma of left antrum. (*A*) L. D. view shows destruction of left L. D. and normal right L. D. (arrow). (*B*) Laminogram demonstrates destruction of the wall of the antrum posteriorly.

some cloudiness of the right ethmoid air cells. The view for L. D. showed destruction of the L. D. of the right maxillary antrum (Fig. 7; and 8, *A* and *B*). This was confirmed by tomography. Biopsy showed right antral epidermoid carcinoma.

Case II. Extensive meningioma of right middle fossa with unusually marked bone erosion. S. S., a 69 year old female, was admitted to the University of Virginia Hospital for evaluation of progressive exophthalmos over the preceding 2 years. There was also severe diminution of visual acuity. On examination, there was marked unreducible and nonpulsatile exophthalmos on the right side. There was diminution of right eye movement. Plain roentgenograms of the skull showed a rarified sella turcica and ill defined opacity of the sphenoid sinus. There was erosion of the tip of the right petrous bone and marked destruction of both wings of the spheroid on the right. Views for the L. D. were obtained. The patient was difficult to examine and the angle used was less than usual; however, there was evidence of destruction of the L. D. on the right side (Fig. 9; and 10). This finding was verified by tomography. At operation, there was an extensive meningioma of the right middle fossa extending to the sphenoid sinus and right orbit.

Case III. Undifferentiated carcinoma arising

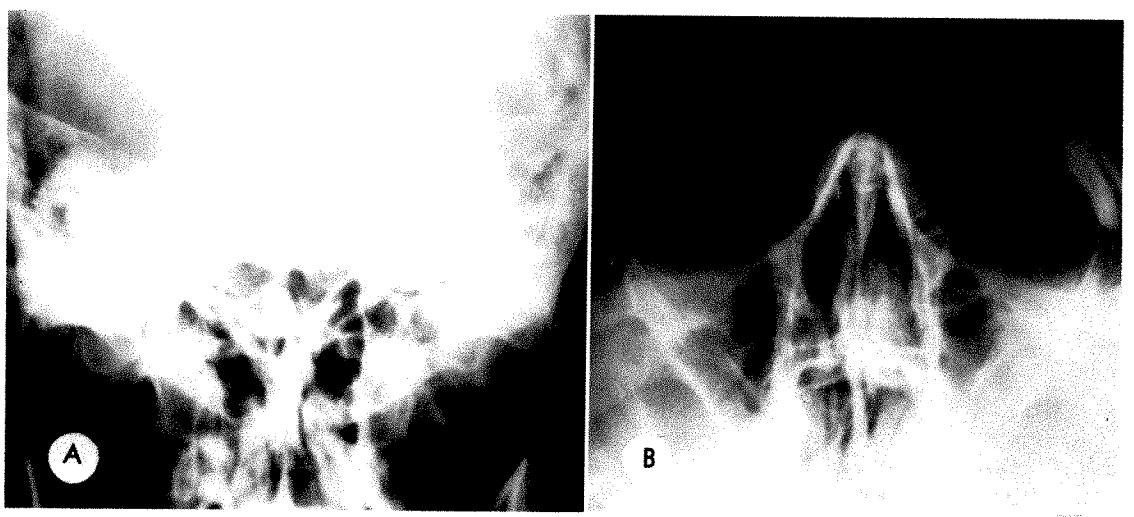


Fig. 13. Mucosal thickening of left antrum. (*A*) L. D. view reveals mucosal thickening adjacent to the L. D. (*B*) Waters' view of same case shows some opacity of the left maxillary antrum.

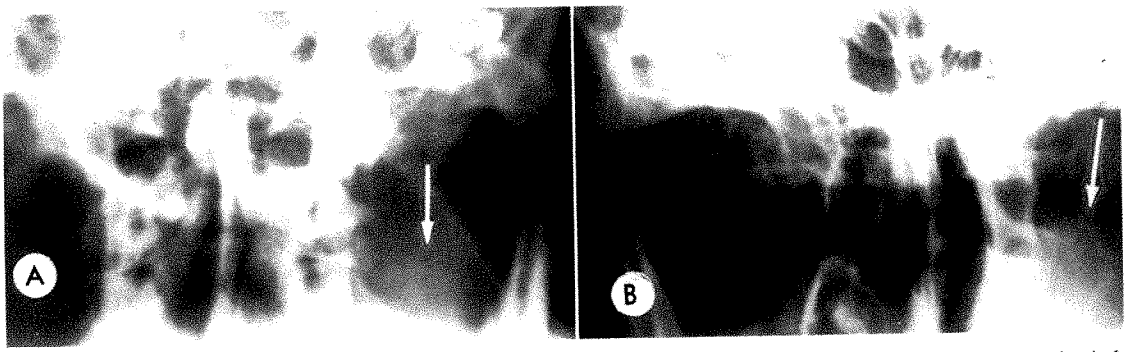


Fig. 14. Mucous polyps. (*A*) L. D. view shows the posterior superior border of a mucous polyp in the left antrum (arrow). (*B*) Another case. L. D. view shows a left maxillary polyp (arrow).

in the left maxilla and nasopharynx. H. B., a 14 year old female, was admitted to the University of Virginia Hospital, January 4, 1968. A prior admission $2\frac{1}{2}$ years before for a mass in the left neck showed atypical Hodgkin's disease. In July, 1967, another biopsy of a right posterior cervical mass showed undifferentiated malignant tumor. The patient then received 1,000 r in 2 days in July, 1967, to the left neck. The patient signed out January 20, 1968 before completion of the treatment. One month before the second admission, the patient noted progressive enlargement of the left face and protuberance of the left eye which was blind. The Waters' view showed an opaque left antrum and erosion of the zygoma and anterior lateral part of the antrum. The L. D. view showed destruction of L. D. on the left confirmed by tomography (Fig. 11, *A* and *B*).

Case iv. Reticulum cell sarcoma of left antrum. T. B., a 71 year old male, was admitted to the University of Virginia Hospital, August 17, 1967. In August, 1965, he developed left cervical lymphadenopathy which was biopsied and reported as reticulum cell sarcoma. He was given 5,000 r in 4 weeks to the left neck.

On August 17, 1967 a nasal polyp was removed and showed reticulum cell sarcoma. In September, 1967, routine plain roentgenography of the paranasal sinuses demonstrated a cloudy left antrum and ethmoidal air cells.

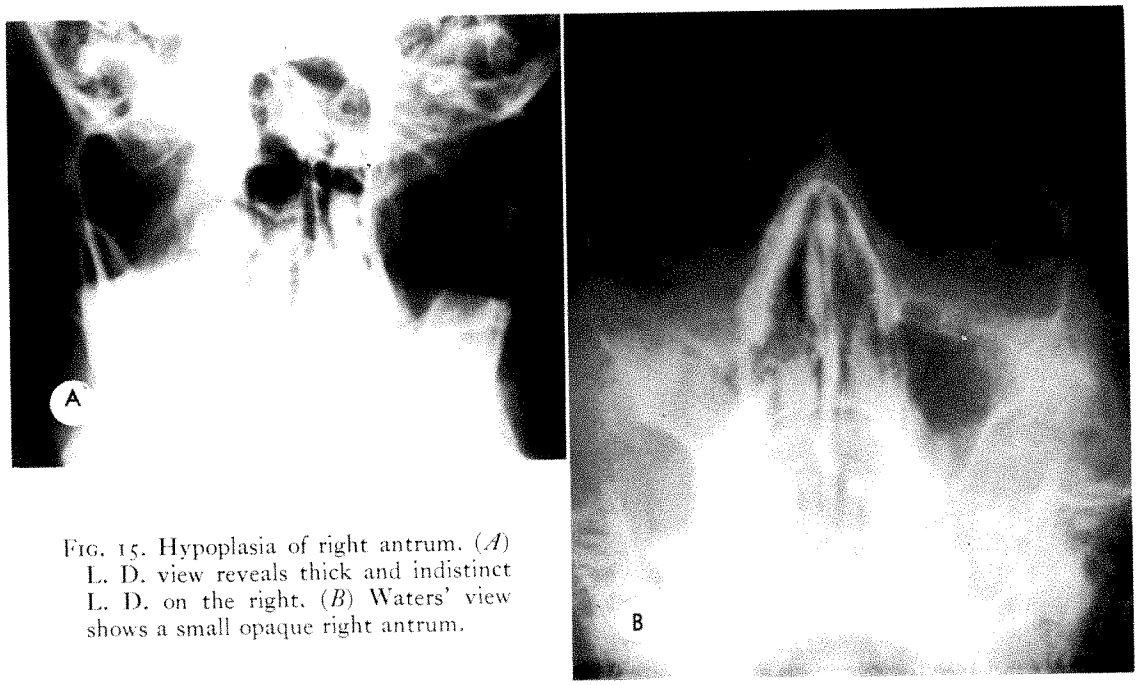


Fig. 15. Hypoplasia of right antrum. (*A*) L. D. view reveals thick and indistinct L. D. on the right. (*B*) Waters' view shows a small opaque right antrum.

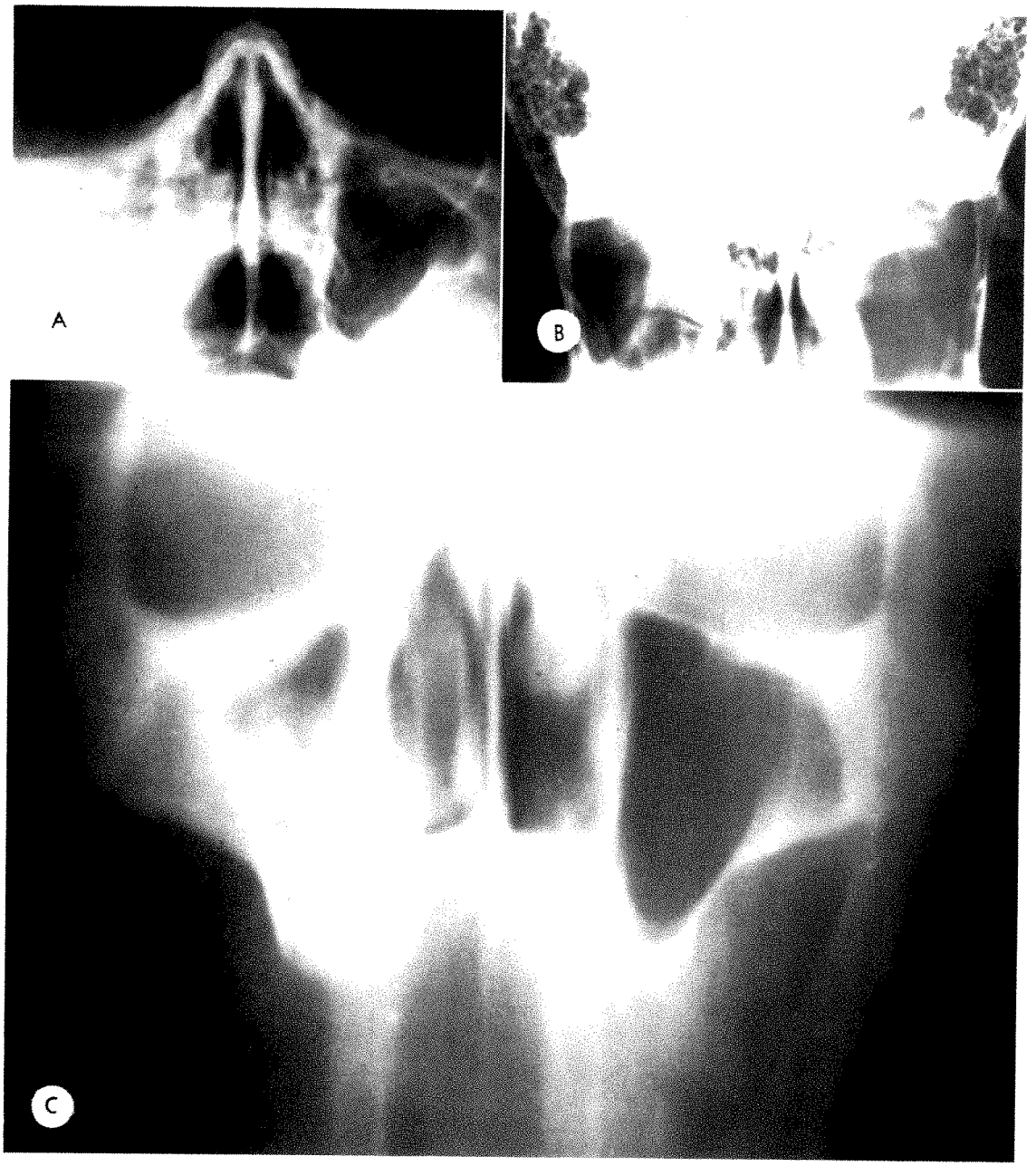


FIG. 16. Possible dentigerous cyst of the right antrum. (*A*) Waters' view shows opaque right antrum with a small density in its lower part. (*B*) L. D. view reveals poorly defined thick right L. D. and normal left L. D. (*C*) Laminogram shows the opaque right antrum with a density possibly representing a tooth in a dentigerous cyst.

He was given 4,000 r to the nose in 4 weeks.

On his admission to the University of Virginia Hospital, he had obstruction of the left nasal air passage and left ocular displacement. The Waters' view showed an opaque left antrum with erosion of the anterior and inferior walls. The L. D. view revealed erosion of the left L. D. This was also demonstrated by tomography (Fig. 12, *A* and *B*). Biopsy of the left antrum disclosed reticulum cell sarcoma. A left inferior meatal antrostomy was performed,

and the patient was referred for cobalt 60 teletherapy to the left antrum.

Inflammatory Lesions. Mucosal thickening sometimes can be seen in the L. D. view (Fig. 13, *A* and *B*). In addition, polyps can be seen in this view in some cases where only a homogeneous opacity of the antrum was noted in the Waters' view (Fig. 14, *A* and *B*).

DISCUSSION

During the last year, we have been using the L. D. view to show the posterior superior surface of the maxillary antrum. This additional view has proved useful in two conditions:

(1) For investigation of facial fractures. This view can be obtained with the patient in the supine position without added discomfort; the extent of the maxillary fractures can be assessed with greater accuracy at an early stage.

(2) In the diffuse opaque maxillary antrum. In these cases, the L. D. view is helpful in detecting posterior erosions in cases of neoplasm, or may reveal a large polyp producing the antral opacity.

In most cases, the L. D. can be clearly seen as a well defined continuous line, provided the patient's head is straight and the film is well exposed. However, the L. D. becomes hazy and ill defined with excessive thickening or hypoplasia of the antrum. We have had experience with 2 such cases (Fig. 15, *A* and *B*; and 16, *A-C*).

We do not intend to suggest that this view be part of the standard routine examination of the paranasal sinuses, but rather that it serve as a source of supplementary information in cases of trauma to the antrum where further definition of the fracture is desirable, and in cases of diffuse opacification of the antrum where this view may provide additional information with regard to the etiology of the opacity.

SUMMARY

A special frontal view for the roentgenographic examination of the maxillary antra is described. In this view, the posterior surface of the maxillary antrum bordering the inferior orbital fissure appears as a thin, dense, continuous line, the lamina dura (L. D.).

The usefulness of this view in different pathologic lesions in the maxillary antra is illustrated. It has proven to be most helpful in facial fractures and in cases of diffuse opacity of undetermined etiology.

Theodore E. Keats, M.D.
Department of Radiology
University of Virginia Hospital
Charlottesville, Virginia 22901

REFERENCE

1. Hartman, E., and Gillies, E. Roentgenologic Diagnosis in Ophthalmology. J. B. Lippincott Company, Philadelphia, 1959, pp. 57–61.

TOMOGRAPHY OF THE TEMPORAL BONE IN PAGET'S DISEASE*

By JERRY P. PETASNICK, M.D.
CHICAGO, ILLINOIS

PAGET'S disease of bone is a chronic, progressive disease of unknown etiology occurring in approximately 3.0 per cent of patients over the age of 40.[2,18] Skull involvement alone or in association with changes elsewhere in the skeleton is quite common and is exceeded in frequency only by involvement of the pelvis and femurs. The incidence of skull involvement in reported series varies from 28 to 70 per cent;[3,5,11,12,13] however, changes limited to the skull are less frequent. Ranniger has found an 11 per cent incidence of Paget's disease limited to the skull in a series of 349 patients, 114 of whom had skull involvement.[11] Although the changes of Paget's disease in the skull are well recognized, relatively little is known about the roentgenographic findings in the temporal bone. Gutman and Kasabach[6] reported involvement of the base of the skull in 7 of 82 patients with Paget's disease elsewhere in the skull and concluded that the base of the skull was involved only when advanced roentgenographic changes were present in the cranial vault. These same authors, in reviewing the findings in 47 patients with osteoporosis circumscripta, reported changes localized to the temporal bone in only 1; 10 patients had diffuse involvement of the entire calvarium, including the temporal bones.[8] The changes observed in the petrous pyramids on conventional roentgenograms may vary from diffuse demineralization to extensive sclerosis. Valvassori,[16] however, has demonstrated tomographically that involvement of the petrous pyramids results in demineralization regardless of the appearance of the petrous pyramids on conventional roentgenograms.

Otologic interest in Paget's disease stems from the resultant hearing loss. Paget's disease and otosclerosis were initially felt to be related entities because of the similarity of otologic symptoms; however, this has not been substantiated histologically.[7,15,18] Moreover, Lindsay and Perlman[9] have pointed out differences in the clinical course of these two entities. Paget's disease usually occurs in late adult life and involves other bones, whereas otosclerosis rarely has its onset after middle age and is limited to the otic capsule. Otologic changes, initially described by Otto Meyer,[10] are a well-recognized finding in patients with advanced skull changes and at times may be the presenting complaint. Hearing loss occurs most frequently; however, patients may complain of vertigo and tinnitus.

Histologic studies, particularly those of Wilson and Anson[18] and Tamari,[15] indicate that the progression of changes in the petrous portion of the temporal bone is similar to that observed elsewhere and that the compact bone in the otic capsule is relatively resistant to the pathologic process. The histologic data are sparse, however, and there are insufficient data relating the pathologic changes to the clinical findings. In view of the changes previously reported by Valvassori,[16] it was thought that tomography would make it possible to categorize changes in the petrous pyramids of these patients which could be compared with the audiometric and vestibular findings.

MATERIAL

Tomographic examinations of both petrous pyramids were obtained in 23 patients with roentgenologic changes of Paget's disease in the skull. Fourteen patients were examined because of known otologic in-

* From the Department of Radiology, The University of Chicago, Chicago, Illinois.

volvement. The otologic and roentgenographic findings in these patients have been discussed previously.[1] The remaining 9 patients were primarily unselected patients referred to the Department of Radiology for examinations unrelated to their Paget's disease. In several of these patients, however, otologic symptoms were present. Audiometric and vestibular studies were available in 17 patients.

RESULTS

The tomographic findings varied from minimal demineralization of the petrous apex to demineralization of the entire petrous pyramid, including the otic capsule (Fig. 1–5), and appeared to correlate grossly with the degree of skull involvement. A small area of sclerosis was present in 1 patient treated with sodium fluoride prior to our initial examination. In the remainder of the patients, no area of sclerosis could be identified despite the presence of extensive areas of sclerosis in the skull (Fig. 6, *A* and *B*). Thirty-six of the 46 petrous pyramids examined had partial or complete demineralization of the cochlea and 32 had changes in the remainder of the otic capsule. Involvement of the internal auditory canals consisted of demineralization of the walls without evidence of narrowing (Fig. 3, *A* and *B*). In patients with extensive involvement, the internal auditory canal was no longer identifiable as a distinct structure (Fig. 4, *A* and *B*; and 5, *A* and *B*). Marginal or complete thickening of the footplate was present in 18 of the ears examined. The remainder of the ossicular chain was normal in all patients. In patients with extensive involvement, the margins of the external auditory canal and middle ear were demineralized.

Audiometric studies demonstrated a mixed hearing loss in 21 of the 34 ears examined with a low frequency conductive deafness. Sensori-neural deafness was present in 10, conductive deafness in 2, and the remaining 1 ear had normal hearing. As indicated by Clemis *et al.*,[1] the pure tone audiograms could be divided into two distinct groups: (1) A definite high frequency drop; or (2) a relatively flat pattern. Although the configuration was similar for both ears in the patients tested, the degree of hearing loss was often asymmetric. The audiometric findings on 14 of the patients in this group have been presented in detail in a previous report.[1] Twenty-eight of the 31 ears with sensori-neural deafness had cochlear changes. Twelve of the 23 ears with a conductive hearing loss had roentgenographically demonstrable changes in the footplate of the stapes. The middle ear was normal in the remaining patients.

An abnormal caloric response was noted in 10 of the 34 ears tested, all of which had changes in the region of the semicircular canals. In an additional 20, however, the

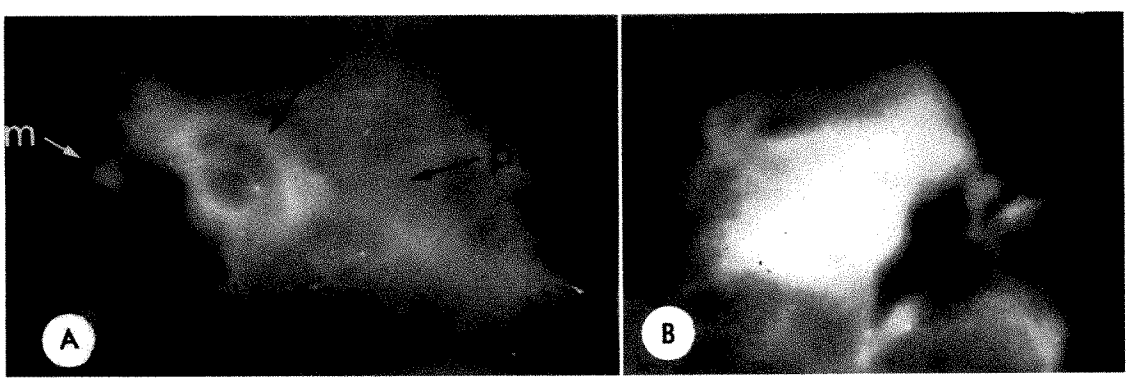


Fig. 1. Patient with minimal involvement of the right petrous pyramid. (*A*) Frontal tomogram of the right petrous pyramid. The petrous apex (p) is demineralized and has a coarse trabecular pattern. The margin of the petrous pyramid is indistinct. The apical turn of the cochlea (c), malleus (m), and middle ear are normal. (*B*) Frontal tomogram of the normal left petrous pyramid.

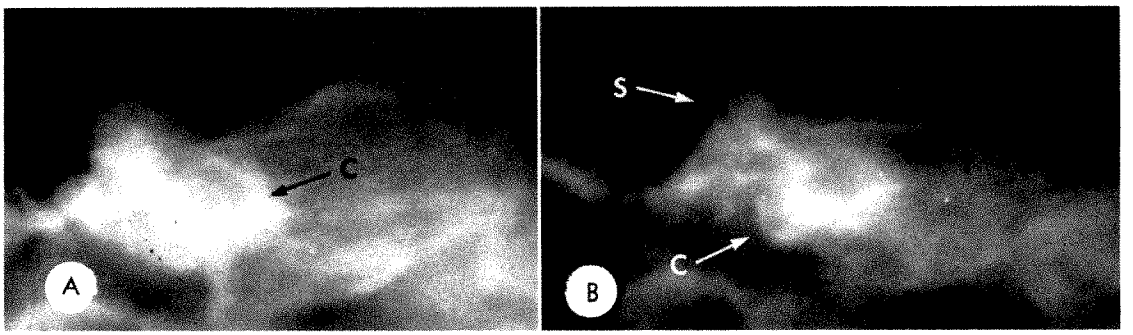


Fig. 2. (*A* and *B*) Frontal tomograms of the right petrous pyramid in a patient with more extensive roentgenographic involvement than that seen in Figure 1. The coarse trabecular pattern and demineralization of the petrous apex are again noted. The cochlea (c) and semicircular canals (s) are normal. The internal auditory canal (i) can be identified; however, its margins are indistinct.

caloric response was normal, whereas the tomograms were definitely abnormal.

DISCUSSION

Involvement of the petrous pyramids in patients with Paget's disease of the skull appears to be more common than previous studies indicate. Conventional roentgenographic examinations were abnormal in 75 per cent of the patients examined and all patients had demonstrable tomographic changes. The roentgenographic changes observed indicate that the medial aspect of the petrous pyramid is the initial site of involvement, followed by progressive involvement of the internal auditory canal and otic capsule. These findings are in agreement with the histologic observations of Wilson and Anson[18] that the otic capsule is relatively spared until advanced changes are present in the remainder of the petrous pyramid. Moreover, Tamari[15] has indicated, on the basis of histologic studies, that the bone changes in the petrous pyramid begin in areas best supplied with marrow tissue, such as the spongy bone of the petrous pyramid and mastoid. The labyrinthine capsule, due to its almost marrowless structure, is the least susceptible. Involvement of the labyrinthine capsule, when present, begins in the outer periosteal layer which, because of its vascularity and small marrow spaces, is amost completely reconstructed. The middle endochondral layer with its small and scanty vessels and its cartilaginous enclosures is more resistant. The replacement of this middle layer becomes effective because of an invasion of

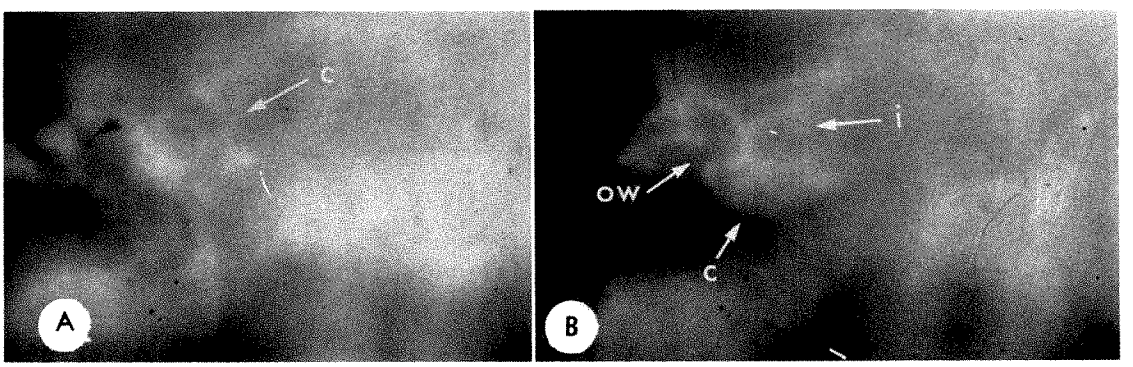


Fig. 3. Patient with extensive involvement of both petrous pyramids. (*A* and *B*) Frontal tomograms of the right petrous pyramid demonstrate demineralization of the petrous apex and margins of the internal auditory canal (i). There is demineralization of the apical and basilar turns of the cochlea (c). In *B* the oval window is clearly seen and appears normal (ow).

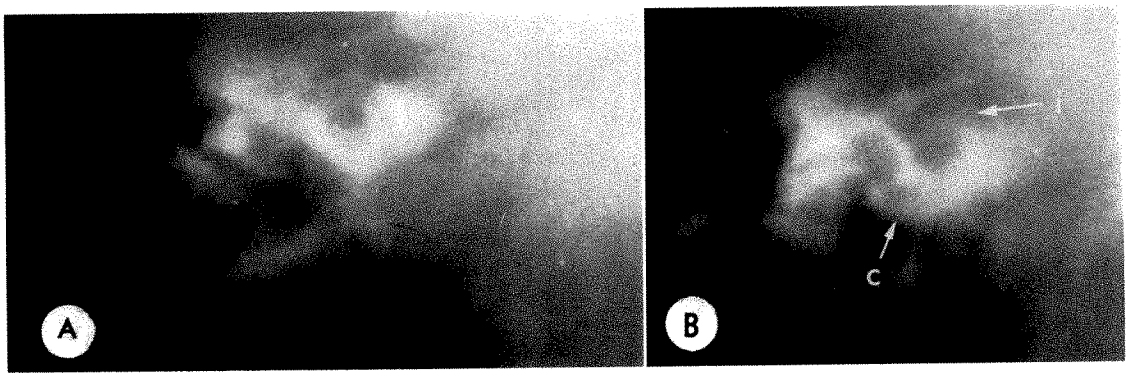


Fig. 4. (*A* and *B*) Extensive involvement of the right petrous pyramid with demineralization of the petrous apex and walls of the internal auditory canal (i). The basilar turn of the cochlea (c) is demineralized. The margin of the petrous apex is no longer identifiable.

the Paget's bone from the periosteal layer. The greatest resistance is in the endosteal layer, which is the last layer to be involved. With extensive involvement, these three layers can no longer be distinguished.

Histologically, the changes in the petrous pyramid are similar to those observed elsewhere in the skeleton, with extensive resorption of bone followed by rapid and irregular bone deposition.[6,15,18] As a consequence, there is a transformation of the normal, smooth, lamellar structures into a mosaic pattern made up of small fragments irregularly arranged. The total thickness of the altered bone is increased, but the new bone has a more porous appearance than that of the bone it replaces. The Paget's bone thus formed may appear sclerotic on conventional roentgenograms. However, Valvassori has suggested that the increased density is due to thickening of the bone which is otherwise demineralized, as shown in the thin tomographic sections.[16] These observations are further substantiated by the fact that the petrous pyramids were demineralized in all the patients examined.

Studies by Lindsay and Perlman,[9] Sparrow and Duvall,[14] and Clemis *et al.*[1] indicate that the hearing loss is most frequently of the mixed type. Sensori-neural loss has been attributed to: platybasia and basilar impression with torsion of the eighth nerve; deformation of the nervine canals and stretching of nerve fibers; atrophy and degeneration of the basilar membrane;[15] and compression of the nerves and vessels in the internal auditory canal.[4] The histologic and roentgenologic studies, however, indicate that cochlear involvement is present in patients with sensori-neural deafness.

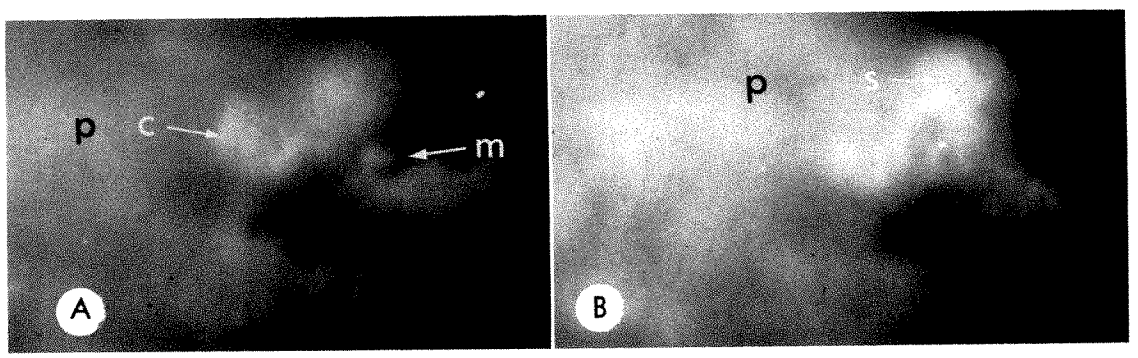


Fig. 5. (*A* and *B*) Far advanced involvement of the left petrous pyramid with extensive demineralization of the petrous apex (p) and otic capsule. The internal auditory canal cannot be identified as a distinct structure and only portions of the cochlea (c) and semicircular canals (s) can be seen. The middle ear and malleus (m) are normal.

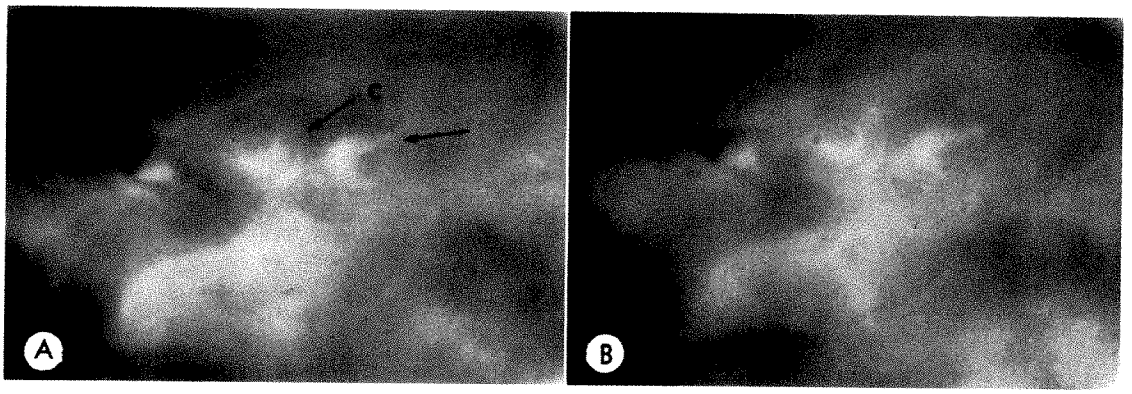


FIG. 6. Patient with far advanced Paget's disease treated with sodium fluoride. In the right petrous apex (*A* and *B*) there is an area of sclerosis (arrow) just medial to the cochlea (c). This is the only example of sclerosis noted in the patients studied and presumably is due to the sodium fluoride therapy. There is extensive demineralization of the entire petrous pyramid. (Tomograms courtesy of Dr. G. Valvassori.)

The involvement of the internal auditory canal appears to be primarily the result of demineralization of the surrounding bone with resultant loss of the internal auditory canal as a clearly identifiable structure. There was no evidence of narrowing of the internal auditory canals in the patients examined. Moreover, Clemis *et al.*[1] found no evidence of a retrocochlear lesion in their group of patients, 14 of whom are included in the current series. Although the presence of a sensori-neural hearing loss can be predicted from the tomographic examination in most cases, there does not appear to be a good correlation between the roentgenologic findings and the severity of the hearing loss. In comparing the audiometric and tomographic findings in the individual ears examined, several instances were observed in which the hearing loss was less in ears with extensive involvement of the cochlea than in those with minimal to moderate changes. These findings might be explained by the observation that Paget's disease is primarily a disease of bone and involves the membranous labyrinth secondarily. Histologic studies have indicated that where the Paget's process involves the otic capsule it proceeds from outward in.

In one patient with moderate involvement of the skull and minimal demineralization of the left petrous pyramid, there was a bilateral, symmetric, flat, 60 decibel, pure sensori-neural hearing loss. On this basis, one might speculate that Paget's disease may be active but roentgenographically subclinical in the temporal bone. More likely, however, the hearing loss is of unknown etiology and unrelated to the patient's Paget's disease.

Roentgenographic changes in the region of the footplate of the stapes and oval window are accompanied by a conductive hearing loss. However, such changes were demonstrable in only 52 per cent of the patients with conductive deafness. Explanations for the conductive loss include sequelae of previous infection, coexisting otosclerosis, stapes fixation by Paget's disease, and the possibility of an audiometric artifact wherein acuity of hearing by bone conduction influences the threshold for low tones by air conduction.[1]

The vestibular function remains intact for a long time and there is no correlation between roentgenographic changes and vestibular findings. One might speculate that the increased vascularity of the Paget's bone changes the bone conduction and delays the reaction to heat and cold.

The roentgenologic differentiation of Paget's disease and labyrinthine otosclerosis should present little problem. In Paget's disease, the changes in the otic capsule are almost always accompanied by involvement of the remainder of the petrous pyramid, whereas labyrinthine otosclerosis is confined to the otic capsule.[17] Moreover,

the sclerotic foci often present in labyrinthine otosclerosis are not seen in Paget's disease.

SUMMARY

Polytomographic examination of the temporal bone in 21 patients with Paget's disease of the skull has demonstrated roentgenographic changes in all patients examined, ranging from minimal demineralization of the petrous apex to demineralization of the entire petrous pyramid. Twenty-nine of the 42 temporal bones examined had partial or complete demineralization of the cochlea and 24 had changes in the remainder of the otic capsule. In addition, marginal or complete thickening of the footplate of the stapes was present in 12 of the ears examined.

Audiometric studies indicate that sensori-neural deafness is most common. However, a significant number of patients have a low frequency conductive hearing loss. The presence of a sensori-neural hearing loss can be predicted in most cases from the tomographic examination. However, two-thirds of the patients with conductive deafness had no roentgenographic changes in the middle ear. The tomographic findings bear no relationship to the presence or absence of vestibular symptoms.

Differentiation from labyrinthine otosclerosis should pose no problem when changes are present in areas other than the otic capsule.

Department of Radiology
University of Chicago
950 East 59th Street
Chicago, Illinois 60637

REFERENCES

1. Clemis, J. D., Boyles, J., Harford, E. R., and Petasnick, J. P. Clinical diagnosis of Paget's disease of temporal bone. *Ann. Otol., Rhin. & Laryng.*, 1967, *76*, 611–623.
2. Collins, D. H. Paget's disease of bone; incidence and subclinical forms. *Lancet*, 1956, *2*, 51–57.
3. Dickson, D. D., Camp, J. D., and Ghormley, R. K. Osteitis deformans; Paget's disease of bone. *Radiology*, 1945, *44*, 449–470.
4. Griffey, L. E. Temporal bone in Paget's disease. *Ann. Otol., Rhin. & Laryng.*, 1960, *69*, 178–183.
5. Gutman, A. B., and Kasabach, H. Paget's disease (osteitis deformans); analysis of 116 cases. *Am. J. M. Sc.*, 1936, *191*, 361–380.
6. Jaffe, H. L. Paget's disease of bone. *Arch. Path.*, 1933, *15*, 83–131.
7. Jenkins, G. J. Otosclerosis and osteitis deformans; pathological and clinical comparison. *J. Laryng. & Otol.*, 1923, *38*, 344–353.
8. Kasabach, H. H., and Gutman, A. B. Osteoporosis circumscripta of skull and Paget's disease; 15 new cases and review of literature. Am. J. Roentgenol. & Rad. Therapy, 1937, *37*, 577–602.
9. Lindsay, J. R., and Perlman, H. B. Paget's disease and deafness. *Arch. Otolaryng.*, 1936, *23*, 580–587.
10. Meyer, O. Demonstriert die Mikrophotogramme von zwei Fällen von Otosklerose mit vier Schläfenbeinen? *Internat. Zentralbl. f. Ohrenh.*, 1913, *11*, 530–531.
11. Ranniger, K. Personal communication.
12. Rosenkrantz, J. A., Wolf, J., and Kaicher, J. J. Paget's disease (osteitis deformans); review of 11 cases. *A.M.A. Arch. Int. Med.*, 1952, *90*, 610–633.
13. Schmorl, G. Über osteitis deformans Paget. *Virchows Arch. path. Anat.*, 1932, *283*, 694–751.
14. Sparrow, N. L., and Duvall, A. J., III. Hearing loss and Paget's disease. *J. Laryng. & Otol.*, 1967, *81*, 601–611.
15. Tamari, M. Histopathologic changes of temporal bone in Paget's disease. *Ann. Otol., Rhin. & Laryng.*, 1942, *51*, 170–208.
16. Valvassori, G. E. Laminography of the Temporal Bone. Book II. In: Radiographic Atlas of the Temporal Bone. American Academy of Ophthalmology and Otolaryngology, 1964.
17. Valvassori, G. E. Radiologic diagnosis of cochlear otosclerosis. *Laryngoscope*, 1965, *75*, 1563–1571.
18. Wilson, J. G., and Anson, B. J. Histologic changes in temporal bone in osteitis deformans (Paget's disease). *Arch. Otolaryng.*, 1936, *23*, 57–77.

THE SUPRACONDYLAR PROCESS AND ITS FRACTURE*

By ALEX NEWMAN, M.D.
PHOENIX, ARIZONA

THE supracondylar process of the humerus is an anomalous beak-like bony projection of variable size on the anteromedial surface of the distal humerus with its point directed downwards, forwards, and medially. It is found 5 to 7 cm. above the medial epicondyle and is joined to it by a band of fibrous tissue. Through the arch thus formed pass the median nerve and the brachial artery or one of its branches. The process itself may give insertion to a portion of the coracobrachial muscle and may also give origin to the pronator teres muscle.[4] The supracondylar process, also called the supracondyloid, supra-epitrochlear, epicondylar, or epicondylic process, is a rudimentary homologue of the supracondylar foramen found in lower animals; it is found in many primate mammals and most marsupials and in many carnivores, especially felines.

Roentgenograms of the elbow or distal

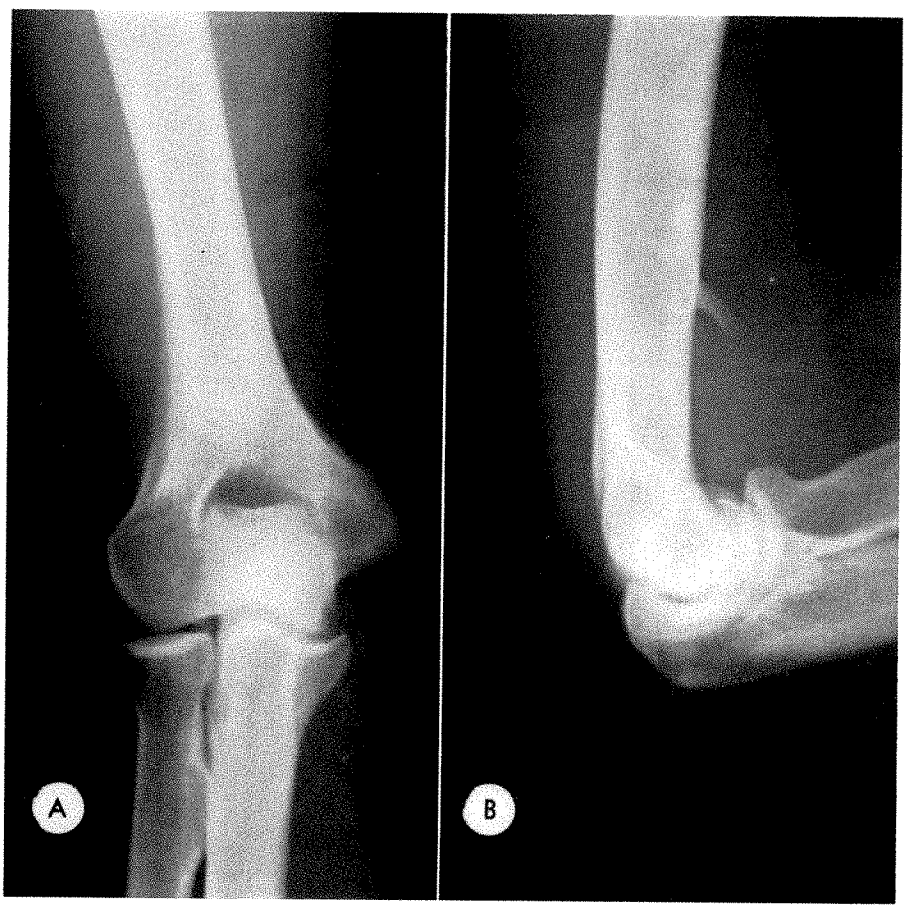


FIG. 1. (*A* and *B*) Typical roentgenographic appearance of a supracondylar process. Note that in the anteroposterior projection (*A*) the process is almost completely hidden by the distal shaft of the humerus.

* From the Department of Radiology, Maricopa County General Hospital, Phoenix, Arizona.



Fig. 2. Slightly oblique projection demonstrates the supracondylar process into sharp profile.

humerus readily demonstrate the supracondylar process; however, in the routine anteroposterior projection, a well developed process may be obscured by the humerus or may be seen only as a slight osseous protrusion from the medial aspect of the humerus (Fig. 1, *A* and *B*). A slightly oblique projection invariably shows the supracondylar process to best advantage (Fig. 2).

This process has been of more interest to anatomists and anthropologists, because of a possible link to the origins and relations of the human races, than to physicians. In 1818 and 1819 Tiedemann[19,20] reported his extensive studies on the occurrence of this process in apes and monkeys. Knox[8] in 1841 first reported its occurrence in man. Struthers[13,14] published extensive studies of this process in man with special reference to its variation and development.

Subsequently, various anatomists and anthropologists began to study the incidence of the supracondylar process in man and the various races of man as well as social strata. The reported incidence has varied from 0.6 per cent to 2.7 per cent. Gruber[5,6] found the process in 2.7 per cent of the cadavers he studied. Testut[18] noted this anomaly in 1 per cent of his specimens. Terry [15–17] was the first to study the incidence of this process in living man utilizing the then new medium of roentgen ray; he reported an incidence of 1.16 per cent in the white population (6 out of 515) and a markedly lower incidence (1 in 1,000) in Negroes. Hrdlička[7] also reported an extremely low incidence in American Indians and the same incidence in Eskimos as in the whites, but the number of the Eskimo group studied was too low for adequate evaluation. The usual quoted incidence of the supracondylar process as approximately 1 per cent of people of European ancestry is attributed to the work of Terry. Parkinson[12] in a study of 500 unselected individuals found the process in only 2 of these giving an incidence of only 0.4 per cent.

Thus, the incidence of the supracondylar process of the humerus is very low, and, accordingly, the true character of this anomalous entity is often unrecognized if the radiologist is not aware of its existence. This process has erroneously been called an exostosis or osteochondroma. Of greater importance is the fact that, although rare, fracture of this process may occur and may give rise to persistent symptoms and neurologic findings.

Lund[10] in 1930 published the first report of a case of fracture of the supracondylar process. Other authors[2,3,11] reported single cases of such fractures, and Doane[1] and Kolb and Moore[9] reported 2 cases.

The following report presents an additional case of this rare fracture of an uncommon anomaly which required surgical excision.

REPORT OF A CASE

R. B., a 5 year old Mexican-American girl,



Fig. 3. (*A* and *B*) Roentgenograms of the left upper extremity showing a supracondylar process with evidence of a fracture.

fell from a swing on November 12, 1967 injuring the left elbow. She was brought to the emergency room of Maricopa County General Hospital on November 17, 1967 complaining of pain in the elbow aggravated by movement. Physical examination revealed exquisite tenderness on palpation of the distal humerus where a mass was present proximal to the medial epicondyle. Roentgenograms revealed a supracondylar process at the distal shaft of the left humerus with evidence of a fracture line through the process with no significant displacement (Fig. 3, *A* and *B*; and 4). No supracondylar process was found in the opposite or right humerus. Treatment consisted of immobilization by a sling, and the patient was referred to the orthopedic clinic for follow-up.

The patient returned to the orthopedic clinic on November 24, 1967 with no relief of symptoms, and, in addition, radiation of pain into the thumb, index, and middle fingers aggravated by pressure at the fracture site. Median nerve symptoms were intensified on subsequent clinic visits, and the patient was admitted to the hospital. On December 13, 1967, surgical excision of the fractured supracondylar process was performed. Microscopic sections of the surgical specimen demonstrated a reparative process in an osseous mass consistent with a healing fracture (Fig. 5; and 6). The postoperative course was uneventful with complete relief of all symptoms.

The patient was 1 of 10 siblings; all of their elbows were subsequently examined roentgeno-

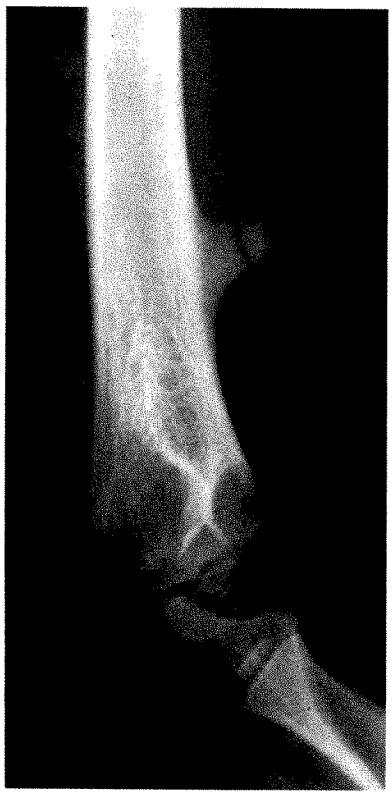


Fig. 4. Enlargement of slightly oblique view showing the supracondylar process and its fracture to best advantage.

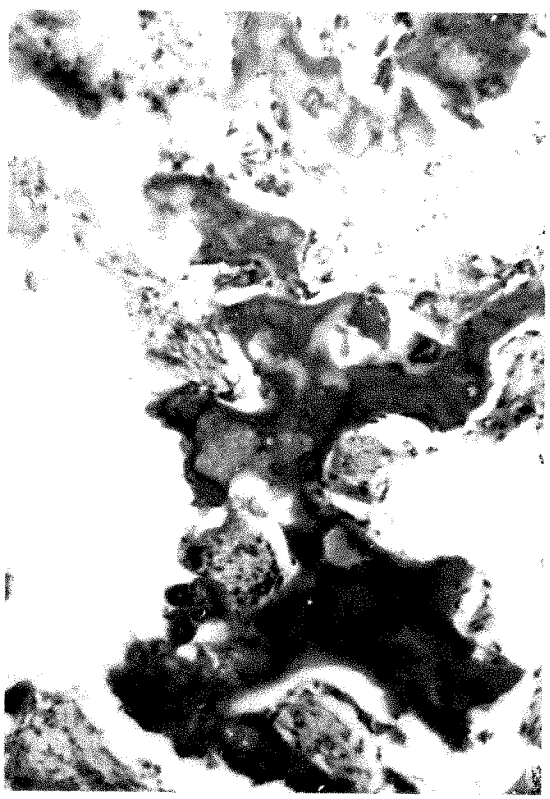
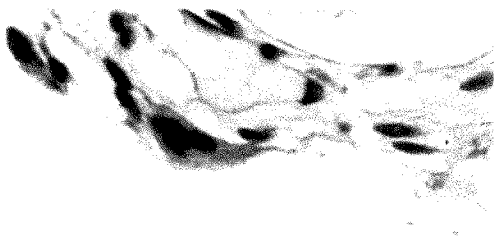


Fig. 5. Low power photomicrograph of an area of bone showing intermixing of old and new bone.



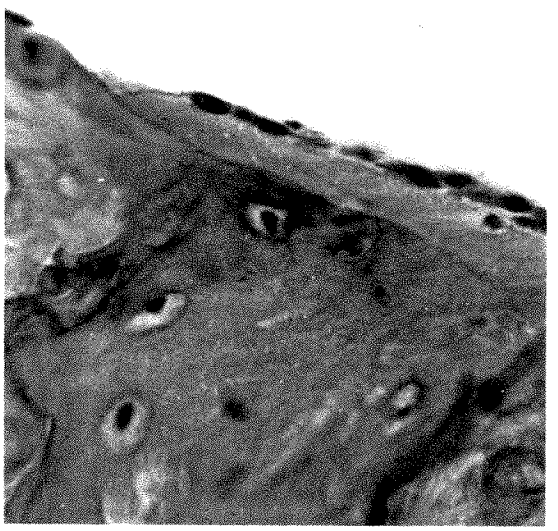


Fig. 6. High power photomicrograph of area of bone repair showing a row of osteoblasts and the cementing line with old bone.

logically, but no trace of a supracondylar process could be found in them or in either of the parents, who were also examined.

DISCUSSION

The incidence of supracondylar process of the humerus is extremely low. In our hospital only 2 such anomalies were found

among the 720 elbows and humeri examined during the past year indicating an incidence of 0.28 per cent, which is definitely lower than that reported by Parkinson[12] and considerably lower than the earlier reports of Terry.[15] If Terry's conclusions[16,17] and Hrdlička's conclusions[7] are correct, then the lower incidence found in our patients may be accounted for by the high percentage of Mexican-Americans, mixtures of American Indians and whites, and Negroes seen in our hospital.

The supracondylar process must be a recessive hereditary trait as indicated by its occurrence in this reported case of 1 in 10 siblings with absence of its presence in both parents. This is contrary to the assumption of Terry.[15]

Inasmuch as the median nerve is usually found in close apposition with the supracondylar process, it is to be expected that fracture of this process could result in a propensity to cause symptoms by compression of the median nerve. In such symptomatic cases, surgical excision of the fracture fragments of the process is the treatment of choice.

SUMMARY

1. The supracondylar process of the humerus is an uncommon congenital anomaly of which radiologists and clinicians should be aware.

2. This process may be fractured and may result in median nerve compression, for which surgical excision is the treatment of choice.

3. The supracondylar process is a recessive hereditary trait; a lower incidence than heretofore reported was noted but may possibly be accounted for by the racial background of the patient population.

Department of Radiology
Maricopa County General Hospital
3435 W. Durango Street
Phoenix, Arizona 85009

REFERENCES

1. Doane, C. P. Fractures of supracondylar process of humerus. *J. Bone & Joint Surg.*, 1936, *18*, 757–759.
2. Ganz, E. Fraktur des Processus supracondylicus humeri. *Röntgen-Praxis*, 1937, *9*, 48.
3. Genner, B. A. Fracture of supracondyloid process. *J. Bone & Joint Surg.*, 1959, *41A*, 1333–1335.
4. Gray, H. Anatomy of the Human Body. Edited by C. M. Goss. Twenty-eighth edition. Lea & Febiger, Philadelphia, 1966, p. 220.
5. Gruber, W. Monographie des Canalis supracondyloideus humeri und der Processus supracondyloidei humeri et femoris der Säugethiere und des Menschen. *Mém. d. sav. étrang. Acad. Imp. Sc.*, 1856, *8*, p. 8.
6. Gruber, W. Zweiter Nachtrag zur Kenntniss der Processus supracondyloideus humeri des Menschen. *Mélang. biol. Acad. Sc.*, 1866–1868, *6*, 573–587.
7. Hrdlička, A. Incidence of supracondyloid process in whites and other races. *Am. J. Phys. Anthropol.*, 1923, *6*, 405–412.
8. Knox, R. On occasional presence of supracondyloid process in human humerus. *Edinburgh M. & S. J.*, 1841, *56*, 125–128.
9. Kolb, L. W., and Moore, R. D. Fractures of supracondylar process of humerus: report of two cases. *J. Bone & Joint Surg.*, 1967, *49A*, 532–534.
10. Lund, H. J. Fracture of supracondyloid process of humerus: report of case. *J. Bone & Joint Surg.*, 1930, *12*, 925–928.
11. Mandruzzato, F. Patologia e chirurgia del processo sopraepitrocleare dell'omero. *Chir. org. movimento*, 1938, *24*, 123–132.
12. Parkinson, C. E. Supracondyloid process. *Radiology*, 1954, *62*, 556–557.
13. Struthers, J. On some points in abnormal anatomy of arm. *Brit. & For. M.-Chir. Rev.*, 1854, *13*, 407–415.
14. Struthers, J. On some points in abnormal anatomy of arm. *Brit. & For. M.-Chir. Rev.*, 1854, *14*, 170–179.
15. Terry, R. J. Study of supracondyloid process in living. *Am. J. Phys. Anthropol.*, 1921, *4*, 129–139.
16. Terry, R. J. On supracondyloid variation in Negro. *Am. J. Phys. Anthropol.*, 1923, *6*, 401–403.
17. Terry, R. J. Racial distribution of supracondyloid variation. *Am. J. Phys. Anthropol.*, 1930, *14*, 459–462.
18. Testut, L. L'apophyse sus-épitrochléene chez l'homme. *Internat. Monatschr. Anat. Physiol.*, 1889, *1*, 391.
19. Tiedemann, F. Über einen am Oberarmbein bei mehreren geschwänzten Affen vorkommenden Kanal und eine damit in Verbindung stehende

besondere Anordnung der Arterien und Nerven des Armes. *Deutsches Archiv für die Physiologie*, 1818, *4*, 544–549.

20. Tiedemann, F. Beiträge zur menschlichen und vergleichenden Anatomie. I. Fernere Untersuchungen über einen bei mehreren Säugethieren am Oberarmbein vorkommenden Kanal, und eine damit in Verbindung stehende Anordnung der Arterien und Nerven. *Deutsches Archiv für die Physiologie*, 1819, *5*, 348–349.

TRIANGULAR CARTILAGE CALCIFICATION IN THE WRISTS: ITS INCIDENCE IN ELDERLY PERSONS*

By WYLIE J. DODDS, M.D.,† *and* HOWARD L. STEINBACH, M.D.
SAN FRANCISCO, CALIFORNIA

CALCIFIED articular or fibrous cartilage in association with primary hyperparathyroidism has been recognized since it was reported independently by Eklöf in 1952[6] and Bywaters in 1959.[2] Calcification of the triangular cartilage in the wrists is common in primary hyperparathyroidism.[5] This cartilage is a triangular fibrocartilage disk which lies in the plane of the wrist. The apex of the triangle is attached to the ulnar styloid and the base to the medial free edge of the distal radius. Because roentgenograms of the hands and wrists are frequently obtained in patients in whom primary hyperparathyroidism is suspected, knowledge of the incidence of calcification of the triangular cartilage, in otherwise normal individuals, becomes important.

MATERIAL AND METHOD

The radiodiagnostic index of the Radiology Department of the University of California San Francisco Medical Center was surveyed for the years 1965 and 1966. During this period 280 patients, 60 years of age or older, were registered for roentgenograms of the wrists, or of the hands and wrists. From this group, patients with gout, rheumatoid arthritis, hyperparathyroidism, and hypercalcemia were exlcuded, since these conditions have been reported in association with cartilage calcification.[3,4,8,11]

The roentgenograms of the 202 remaining patients (63 males and 139 females) were surveyed for the presence of triangular cartilage calcification in the wrist. The mean age for this group was 69.4 years (range, 60 to 89 years). The recorded indications for roentgenograms were: trauma, 85; arthralgia, 53; miscellaneous, 60; and indication not listed, 14. Fractures were demonstrated in 58 instances and moderate to advanced osteoarthritis in 72. In 100 of the 202 patients, roentgenograms had been obtained of both wrists.

RESULTS

Calcification of the triangular cartilage was demonstrated in 5 of the 202 patients (2.5 per cent) (Table 1; Fig. 1 and 2). The mean age of the 5 patients with such calcification was 74.2 years (range, 69 to 87 years), whereas it was 69.4 years (range, 60 to 89 years) for the 198 patients without this calcification. Roentgenograms of both wrists had been obtained in all 5 patients with calcification of the triangular cartilage. The calcification was bilateral in 3 and unilateral in 2. Cartilage calcification of the shoulders or hips in all 5 patients was not evident on roentgenograms of the chest and abdomen. None of the 5 had had roentgenograms of the knees. In 3 of the 5 patients, significant osteoarthritis was present in the wrists. In 1 patient the osteoarthritis was unilateral and appeared to be post-traumatic.

Detailed hospital records, available on all 5 patients with cartilage calcification of the wrists, showed that 3 of the 5 patients had had wrist pain. None had complained of symptoms referable to other joints nor was there a history of renal calculi. In 2 patients, the serum calcium was measured and found to be normal. The uric acid in these 2 was slightly elevated. Nothing in the records of any of the 5 patients suggested gout, pseudogout, or hyperparathyroidism.

DISCUSSION

Joint cartilage may become calcified for unknown reasons, or may be associated with degenerative changes, gout, hemo-

* From the Department of Radiology, University of California School of Medicine, San Francisco, California.
Supported by grants from the U. S. Public Health Service (AM 02589) and the National Institutes of Health (GM 1272).
† Research Fellow, Diagnostic Radiology.

TABLE I

PATIENTS WITH CALCIFICATION OF THE TRIANGULAR CARTILAGE

Case No.	Sex	Age	Symptoms	Roentgenographic Changes	Triangular Cartilage Calcification
I	F	71	Arthralgia	Osteoarthritis	Bilateral
II	M	70	Arthralgia	Post-traumatic arthritis; old fracture, right	Right wrist
III	F	87	None	Osteoarthritis	Bilateral
IV	F	69	None	Short fourth metacarpal	Bilateral
V	F	74	Arthralgia	Osteoarthritis	Right wrist

chromatosis, ochronosis, or primary hyperparathyroidism.[4] A recent review of 91 patients with proven primary hyperparathyroidism disclosed calcified joint cartilage in 18 per cent, most of whom had triangular cartilage calcification in the wrists.[5] In this series osteoarthritis of the wrist was evident in only one instance. Roentgen evidence of osteitis fibrosa, such as subperiosteal resorption or cyst formation, was absent in one-half of these patients.

Cartilage degeneration associated with aging can result in calcification.[10] Bocher *et al.*,[1] in a study of patients averaging 80 years of age, demonstrated a 7 per cent incidence of meniscal or articular cartilage calcification. These authors attributed the calcification to degeneration. In the present series, the 5 instances of cartilage calcification of the wrists are also considered as secondary to degeneration of cartilage. The incidence of 2.5 per cent calcification of the triangular cartilage in an elderly population is low. Perhaps the lower incidence in the wrists (2.5 per cent) compared to that noted by Bocher *et al.*[1] in the knees (7.0 per cent), is related to the difference in the mean age of the two groups (69 *versus* 80 years). It may also be a result of more severe degeneration in the cartilage of the knees from stress of weight bearing.

Pain in the wrist was the complaint of 3 of the 5 patients with triangular cartilage calcification. The arthralgia may have been the result of the coexisting osteoarthritis, however, rather than of the cartilage calcification. In none of the patients was the arthralgia of an acute inflammatory nature.

Because triangular cartilage calcification of the wrists is common in primary hyper-

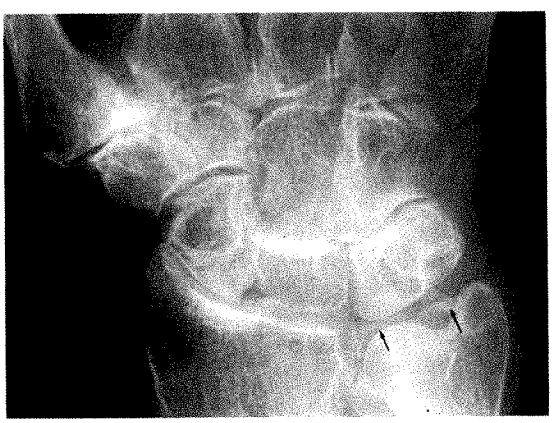


FIG. 1. Case I. The right wrist of a 71 year old woman in whom triangular cartilage calcification was bilateral. Degenerative changes are present in the first metacarpal-greater multangular joint.

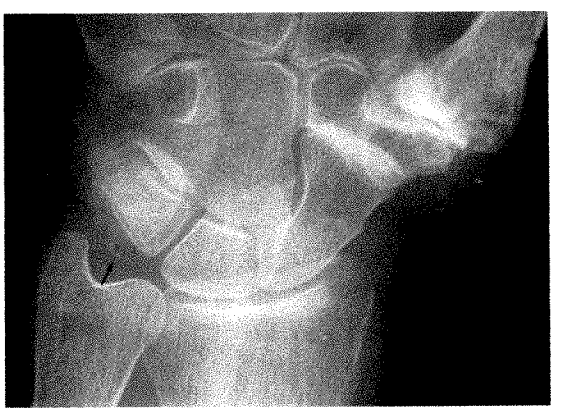


FIG. 2. Case III. The left wrist of an 87 year old woman with bilateral triangular cartilage calcification. Sclerotic degenerative changes are present in the first metacarpal-greater multangular and navicular-greater multangular joints.

parathyroidism but uncommon, even in an aged normal population, its presence when primary hyperparathyroidism is suspected tends to support the diagnosis. If calcification of the triangular cartilage is noted as an incidental roentgen finding, primary hyperparathyroidism should be excluded.

On most of the routine roentgenograms available, the authors could not distinguish degenerative calcification of the triangular cartilage from that seen with primary hyperparathyroidism. McCarty *et al.*[7] and Parlee, Freundlich and McCarty[9] reported that demonstrated linear and punctate calcium deposits in hyaline and fibroarticular cartilage are almost pathognomonic of the calcium pyrophosphate crystals. Degenerative cartilage calcification is believed to be associated with apatite crystals. The roentgen appearance of calcification of the articular cartilage in primary chondrocalcinosis (pseudogout) and that associated with primary hyperparathyroidism is similar. Perhaps if industrial x-ray film, type M, were employed for finer detail, the distinction between degenerative triangular cartilage calcification and that related to primary hyperparathyroidism could be appreciated.

SUMMARY

In an elderly population of 202 patients, with a mean age of 69.4 years, calcification of the triangular cartilage of the wrists was present in 5 patients (2.5 per cent). This finding was thought to be associated with degeneration of the cartilage. Since cartilage calcification in the wrists is a common finding in primary hyperparathyroidism and may occur without roentgen evidence of periosteal resorption, its presence in patients in whom parathyroid hyperfunction is suspected supports the diagnosis. If triangular cartilage calcification is noted as an incidental finding, primary hyperparathyroidism, among other conditions causing cartilage calcification, should be excluded.

Wylie J. Dodds, M.D.
Department of Radiology
University of California
San Francisco Medical Center
San Francisco, California 94122

REFERENCES

1. Bocher, J., Mankin, H. J., Berk, R. N., and Rodnan, G. P. Prevalence of calcified meniscal cartilage in elderly persons. *New England J. Med.*, 1965, *272*, 1093–1097.
2. Bywaters, E. G. L. Discussion: Simulation of rheumatic disorders by metabolic bone diseases. By S. W. Stanbury, A. J. Popert, and J. Ball. *Ann. Rheumat. Dis.*, 1959, *18*, 63–65.
3. Bywaters, E. G. L., Dixon, A. S., and Scott, J. T. Joint lesions of hyperparathyroidism. *Ann. Rheumat. Dis.*, 1963, *22*, 171–187.
4. Dodds, W. J., and Steinbach, H. L. Gout associated with calcification of cartilage. *New England J. Med.*, 1966, *275*, 745–749.
5. Dodds, W. J., and Steinbach, H. L. Primary hyperparathyroidism and articular cartilage calcification. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1968, *104*, 884–892.
6. Eklöf, G. Calcification of menisci in patient with hyperparathyroidism. *Nord. med.*, 1952, *47*, 899–900.
7. McCarty, D. J., Jr., Hogan, J. M., Gatter, R. A., and Grossman, M. Studies on pathological calcifications in human cartilage. I. Prevalence and types of crystal deposits in menisci of 215 cadavers. *J. Bone & Joint Surg.*, 1966, *48A*, 309–325.
8. Moskowitz, R. W., and Katz, D. Chondrocalcinosis coincidental to other rheumatic disease. *A.M.A. Arch. Int. Med.*, 1965, *115*, 680–683.
9. Parlee, D. E., Freundlich, I. M., and McCarty, D. J., Jr. Comparative study of roentgenographic techniques for detection of calcium pyrophosphate dihydrate deposits (pseudogout) in human cartilage. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1967, *99*, 688–694.
10. Urist, M. R. Recent advances in physiology of calcification. *J. Bone & Joint Surg.*, 1964, *46A*, 889–900.
11. Vix, V. A. Articular and fibrocartilage calcification in hyperparathyroidism: associated hyperuricemia. *Radiology*, 1964, *83*, 468–471.

VOL. 105, NO. 4

A STUDY OF INTER- AND INTRA-OBSERVER ERROR IN READING PLAIN ROENTGENOGRAMS OF THE HANDS*

"TO ERR IS HUMAN"**

By JOHN H. BLAND, M.D.,† A. BRADLEY SOULE, M.D.,‡ FREDERICK W. VANBUSKIRK, M.D.,§ ESTELLE BROWN, B.S.,‖ *and* RUTH V. CLAYTON¶
BURLINGTON, VERMONT

THE detailed "blind" reading of plain roentgenograms of the hands is a rewarding if sobering exercise, and points up the reality of what Sir Wilfred Trotter called "the mysterious viability of the false." As part of a larger combined metabolic-rheumatologic-roentgenologic study of plain roentgenograms of the hands, feet and cervical spine, an experiment was designed in which two radiologists and a rheumatologist read 150 pairs of hand roentgenograms (one with, one without comparator bones). Patients were classified according to age, sex, and clinical state. The purpose was to answer the following questions: (1) Does a set of comparator bones roentgenographed simultaneously with the hands aid in the detection of osteoporosis, osteoarthritis and rheumatoid arthritis? (2) What is the frequency of inter- and intra-observer error in reading plain roentgenograms of the hands with and without a comparator bone? (3) What influence, if any, does knowledge of the diagnosis have? (4) Does detectable osteoporosis occur in patients at bedrest for 72 hours following a surgical procedure?

The conclusions were: (1) The set of comparator bones made no statistically significant difference in the roentgenologic detection of osteoporosis, osteoarthritis and rheumatoid arthritis. (2) All readers showed some intra-observer error. Roentgenological signs of osteoporosis, osteoarthritis and rheumatoid arthritis were agreed upon prior to the experiment, but reader differences appeared when the roentgenograms were read blindly. (3) Knowledge of the diagnosis influenced all observers. (4) One reader read 5 per cent of the roentgenograms of the surgical patients as positive for osteoporosis; another read 14 per cent positive, and the third, with a known bias, read 30 per cent positive.

It is obvious that this study is an artificial circumstance, having no correlation in the practice of clinical radiology as each reader was requested to classify his findings as "positive" or "negative." The radiologist is first a physician, then a radiologist. He often reads roentgenograms as "borderline," "questionable," or "suspicious," urging correlation with clinical and laboratory studies, or suggesting further roentgenologic investigation.

METHOD

A set of normal, human, middle finger bones were prepared (third metacarpal, proximal, middle and distal phalanges), using the finger of a healthy 32 year old man killed in an automobile accident. After appropriate fixation and dehydration, the finger bones were embedded in a mixture of paraffin and beeswax of approximately the same roentgenographic

* From the Departments of Medicine (Rheumatology Unit) and Radiology, University of Vermont College of Medicine, Burlington, Vermont.

** Alexander Pope, *Essay on Criticism*, Part II, line 325.

This study was supported by USPHS Training Grant T1-AM-5087, the W. Douglas Burden Grant, and Vermont Chapter Arthritis Foundation.

† Associate Professor of Medicine; Director, Rheumatology Unit; Department of Medicine.
‡ Professor and Chairman, Department of Radiology.
§ Associate Professor of Radiology.
‖ Statistician, Department of Medicine (Rheumatology Unit).
¶ Clinical Assistant, Department of Medicine (Rheumatology Unit).

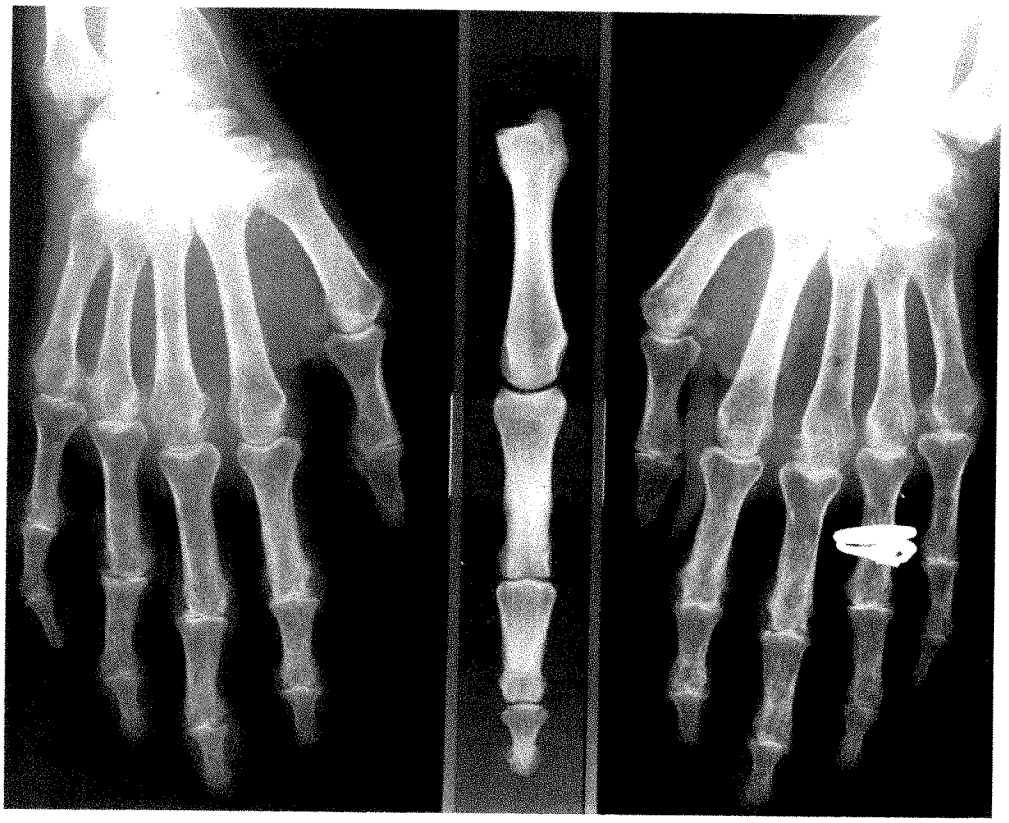


Fig. 1. Hand roentgenograms with comparator bone.

density as human skin and subcutaneous tissue. The embedded bones were enclosed in a plexiglass box (Fig. 1). The comparator bones were roentgenographed by placing the box on the unexposed x-ray film between the patient's hands. Under well standardized conditions the roentgenograms show 4 comparator finger bones of constant roentgenographic density beside the subject's finger bones of unknown density. The question asked was whether the ability of the film reader to recognize decrease in bone density would be affected.

Three groups of 50 subjects' hands were roentgenographed, one roentgenogram without and one with the comparator bone. Group I consisted of 50 people, 25 males and 25 females, healthy and physically active, between the ages of 25 and 45 years; none had a history of skeletal trauma or genetic background of rheumatic disease. Group II consisted of 50 patients, 25 males and 25 females, between the ages of 25 and 45 years, hospitalized for surgical treatment, *i.e.*, appendectomy, herniorrhaphy, hysterectomy, hemorrhoidectomy, or other operations of comparable magnitude. There was no history of skeletal trauma or known rheumatic disease. Hand roentgenograms were taken 48 to 72 hours after operation. Group III was made up of 50 patients with definite or classical rheumatoid arthritis, 25 males and 25 females between the ages of 25 and 55 years.

Roentgenologic signs for the identification of osteoporosis, rheumatoid arthritis and osteoarthritis were agreed upon. Table I lists the criteria. The signs listed were thought to reflect the disorders, but each reader made his diagnostic decisions without specific reference to the signs. We wanted general agreement on such terms as erosions, holes, osteophytes, cysts, coarsening of trabeculae and soft tissue swelling. The readers read each group of roentgenograms separately with knowl-

edge of diagnosis (Table II; Reading A). Then the 3 groups of roentgenograms were randomly mixed and each reader read the roentgenograms "blindly" without knowledge of diagnosis (Table II; Reading B). The films were of the same brand, the same type of developer was used, and the techniques were kept as constant as possible.

RESULTS

Table II records the 3 readers' interpretations of the roentgenograms for osteoporosis, osteoarthritis and rheumatoid arthritis.

Group I (normal hand roentgenograms). The comparator bones did not significantly affect the reading of osteoporosis. When the diagnosis was unknown all observers read osteoporosis positive more often than when they knew the diagnosis. One reader read osteoporosis with diagnosis unknown significantly more frequently with, as well as without, the comparator bones.

Neither the knowledge of diagnosis nor the comparator bones affected the number read as osteoarthritis. The incidence of osteoarthritis is low and there were no significant differences among the readers.

The comparator bones did not affect the

TABLE I

ROENTGENOLOGIC CRITERIA FOR IDENTIFICATION OF OSTEOPOROSIS, OSTEOARTHRITIS AND RHEUMATOID ARTHRITIS

Osteoporosis

1. Generalized decrease in density of all bones of the skeleton
2. Decrease in density predominating in more vascular areas; increased contrast between shafts and ends of bones; translucent areas on either side of the epiphyseal lines
3. Mottled appearances (different from senile osteoporosis which is uniform, gradual in occurrence and more ordered)
4. Translucent intertrabecular spacing; spaces wider, resulting from thinning of trabeculae
5. Decreased opacity of spongiosa due to trabeculae becoming progressively thinner (no destruction of trabeculae as noted in infection)
6. Opacity of compact bone lags behind that of spongiosa
7. Decreased width of cortex
8. Decreased density and width of articular cortex; dash pattern along articular cortex due to varying loss of cortex (observed with magnifying glass); decreased density of subarticular trabeculae; porosis of underlying trabeculae where articular cortex is thinned; translucent zone within articular cortex separating cortex into two thin layers

TABLE I (*Continued*)

Osteoarthritis

1. Earliest change—beak-shaped osteophyte at place of insertion of capsular ligaments to joint margin (uniform density of osteophyte)
2. Loss of cartilage of one-sided irregular character; faults in bone position or alignment; corresponding shifts in lines of stress (different from rheumatoid arthritis which shows uniform loss of cartilage)
3. Separate ossicles noted in capsular ligaments
4. Hypertrophic outgrowths of bone, not beak-shaped or sharp, but bulky, resembling melted wax (Heberden's nodes)
5. Osteosclerosis of subarticular bones
6. Coarsening of trabeculae along lines of stress without thinning of trabeculae
7. Late changes:
   a. gross loss of cartilage
   b. eburnation with pitting of articular surfaces
   c. subarticular cystic degeneration
   d. subluxation
8. Nodules in soft tissue; swelling over hypertrophy in bone

Rheumatoid Arthritis

1. Osteoporosis at first generalized
2. Increase in joint space, early, due to small effusion and swelling and laxity of connective tissues
3. Soft tissue swelling; effusion
4. Osteoporosis, first noted in spongiosa and sub articular cortex, mottled, localized
5. Periosteal elevation best seen on the lateral sides of the metacarpals just below articular cortex
6. Local pattern of osteoporosis predominant in more vascular areas
7. Decreased cartilage of uniform character resulting in decreased joint space
8. Localized osteoporosis of articular cortex and underlying spongiosa; eroded trabeculae
9. Erosions: surface type, pocketed type and enclosed type
10. Subluxation
11. Ankylosis
12. Spikey lipping, secondary osteoarthritis

TABLE II

THE THREE READERS' INTERPRETATIONS OF ROENTGENOGRAMS FOR OSTEOPOROSIS, OSTEOARTHRITIS AND RHEUMATOID ARTHRITIS

	With Control Bone No. Positive					Without Control Bone No. Positive				
	Reading A	Reading B				Reading A	Reading B			
	Diagnosis Known	Diagnosis Unknown	χ^2y*	P	Significant Difference	Diagnosis Known	Diagnosis Unknown	χ^2y*	P	Significant Difference
					GROUP I					
Osteoporosis										
Reader A	2	3	not done	—	no	4	6	not done	—	no
Reader B	7	14	2.5514	.30	no	10	12	not done	—	no
Reader C	2	13	7.8341	<.001	yes	3	12	5.0196	.02	yes
Osteoarthritis										
Reader A	0	2	not done	—	no	1	2	not done	—	no
Reader B	1	0	not done	—	no	4	1	not done	—	no
Reader C	3	0	not done	—	no	0	1	not done	—	no
Rheumatoid Arthritis										
Reader A	1	2	not done	—	no	3	3	not done	—	no
Reader B	0	0	not done	—	no	0	0	not done	—	no
Reader C	2	16	14.4958	<.001	yes, very	3	20	14.4551	<.001	yes, very
					GROUP II					
Osteoporosis										
Reader A	2	1	not done	—	no	3	1	not done	—	no
Reader B	15	9	1.4569	.20	no	15	6	3.8577	.05	yes
Reader C	2	6	1.2228	.30–.20	no	7	8	not done	—	no
Osteoarthritis										
Reader A	3	2	not done	—	no	3	2	not done	—	no
Reader B	2	2	not done	—	no	1	2	not done	—	no
Reader C	2	1	not done	—	no	2	0	not done	—	no
Rheumatoid Arthritis										
Reader A	1	2	not done	—	no	2	1	not done	—	no
Reader B	0	0	not done	—	no	1	1	not done	—	no
Reader C	2	17	12.7355	<.001	yes	5	17	7.0513	<.01	yes
					GROUP III					
Osteoporosis										
Reader A	26	31	.6528	.40	no	27	34	1.5132	.20	no
Reader B	34	37	not done	—	no	29	35	1.0851	.30	no
Reader C	36	43	2.1700	.20–.10	no	45	39	1.8601	.20–.30	no
Osteoarthritis										
Reader A	0	7	5.5300	.02	yes	1	10	6.5373	.01	yes
Reader B	11	7	.6098	.50–.30	no	10	9	not done	—	no
Reader C	1	2	not done	—	no	1	4	not done	—	no
Rheumatoid Arthritis										
Reader A	34	41	1.9200	.20–.10	no	33	35	not done	—	no
Reader B	31	29	not done	—	no	35	25	3.3750	.05†	borderline
Reader C	46	43	not done	—	no	49	45	not done	—	no

* x^2y = Chi squared with Yates Correction for continuity.
† almost .05.

number of roentgenograms read as positive for rheumatoid arthritis. One reader read more roentgenograms positive for rheumatoid arthritis when he did not know the diagnosis than when he did; this was statistically significant. Other readers' results were unaffected by knowledge of the diagnosis.

Group II (surgical patients). The comparator bone made no significant difference in the number of roentgenograms read positive for osteoporosis. One reader with a known bias read osteoporosis more often knowing than not knowing the diagnosis; the difference was statistically significant. The comparator bone made no difference in the reading for osteoarthritis and knowledge of diagnosis had no influence.

The comparator bone did not influence the reading for rheumatoid arthritis. One

reader recorded rheumatoid arthritis significantly more often not knowing the diagnosis.

Group III (rheumatoid arthritis patients). The reading of osteoporosis was not significantly influenced by knowledge of diagnosis or presence of comparator bones. The knowledge of diagnosis significantly influenced the reading of osteoarthritis by one reader. One reader read rheumatoid arthritis positive more often knowing than not knowing the diagnosis. No readings were influenced by the presence of the comparator bone.

DISCUSSION

The capacity of man to make honest errors and perpetuate them is a strange and marvelous characteristic. [9,12,13] Josh Billings' aphorism is well worth its frequent repetition: "It ain't what we don't know that gits us. It's what we do know that ain't so!" The present study amply confirms it.

Humans will perform better if they know they are being tested. The human equation in any diagnostic procedure is difficult or impossible to measure. We know that "we see at one time and not at another" and "to behold is not necessarily to observe." Observer error has been effectively studied in chest roentgenography.[3] We thought that the examination of roentgenograms of the hands would constitute more rigorous study than that of chest roentgenograms. Such is not so.[15]

Roentgenograms constitute a method of recording information. As the film is exposed a certain amount of information is recorded, *i.e.*, a theoretical 100 per cent. It is possible that present roentgenologic techniques may record artifacts of which we are unaware; technical and ocular limitation may constitute immeasurable handicaps. Recognition and retrieval of the information (or misinformation) is the problem to solve. We asked, how much of the recorded information will be retrieved and given meaning? Garland[9,10,11] is a leader in the study of observer error and noted that approximately 20 to 30 per cent of significant information recorded is not recovered. We seek the best means of increasing retrieval of recorded information.

Observer error is not peculiar to medical sciences nor to any one aspect of human endeavor. The literature on observer error discloses a clinically important magnitude that must be expected in interpretation and evaluation of many clinical and laboratory procedures. The existence of diagnostic error may go unappreciated. Paton[14] studied 1,000 cases of myocardial infarction diagnosed clinically; 214 cases came to necropsy and the diagnosis of myocardial infarction was confirmed in only 118. Conversely, myocardial infarction was diagnosed at necropsy in 52 patients in whom it was not suspected clinically. The accuracy rate for the diagnosis of myocardial infarction was about 44 per cent. Fletcher[8] requested 8 internists to examine the chests of 20 patients with pulmonary emphysema. The aim was to assess the validity of well-known physical signs. Agreement on the presence of the most simple signs was only 15 per cent. About 66 per cent of the physical signs were agreed upon, slightly better than chance. The observer's integration of separate signs in the diagnosis of emphysema was no better than the use of physical signs.

Derryberry[7] asked 5 pediatricians to classify 221 children in respect to their nutritional status. Physical examination and diagnostic aids were used as desired. The 5 examiners agreed on the diagnosis of malnutrition in only 7 children. There were 90 children in whom one or another of the examiners diagnosed malnutrition. Cochrane and Garland[3] studied observer error in recording medical histories; 4 doctors interviewed 993 miners "soliciting the same information," *i.e.*, asking the same questions. Common symptoms such as cough, presence of sputum, dyspnea and pain were inquired into. They concluded that there were wide variations in the description of disease and the history recorded was very strongly biased by the attitude and back-

ground of the recorder. Davies[6] studied variances in interpretation of electrocardiograms. Nine experienced physicians read 100 electrocardiograms; only 3 categories were reported, *i.e.*, normal, abnormal and myocardial infarction. The tracings were read and several weeks later read again. There was disagreement in all 3 categories. There was as much difficulty between normal and abnormal as between abnormal and myocardial infarction. Each observer's working definition of "abnormal" varied. The diagnostic value of the electrocardiogram is apparently less than realized. Belk and Sunderman[1] studied predictability of chemical analyses of standard solutions in 59 hospital clinical laboratories. Wide variation was noted and the gross error varied from 5 to 28 per cent. Birkelo *et al.*[2] report that in reading both 35 mm. screening roentgenograms of the chest and 14×17 inch roentgenograms, 5 radiologists underread or missed 25 per cent of the positive roentgenograms in each series and had a 20 per cent intra-observer error when the roentgenograms were re-read 3 months later. Dual interpretation significantly reduced under-reading.[5]

Most clinicians regard the pathologist as having a higher degree of predictability in his conclusions than physicians in other branches of medicine. Diagnoses are "confirmed" by histologic diagnosis, biopsy, resection or postmortem studies. Few studies have been made of observer error in pathology. Pathology has become the yardstick to measure all other diagnostic errors. Cole[4] reported a study comparing clinical, roentgenologic, pathologic and surgical capabilities in making the diagnosis of gastric lesions. Eight microscopic sections of organic gastric lesions taken from surgical and autopsy specimens were presented to some or all of an eminent group of 23 pathologists. They were asked to decide whether the lesion was malignant; if so, to identify the type of malignancy and lastly, to state criteria on which their opinion was based. There was a surprising divergence of opinion. As in other studies of observer error there was about a 25 per cent difference of opinion among representative pathologists as to whether the lesion was malignant. Dr. James Ewing thought that such a difference of opinion would occur in about 20 per cent of cases.

The present study adds to the small body of information on observer error, confirming the experience of previous investigators; observer error is an important feature in clinical practice of all branches of medicine thus far tested; the phenomenon is probably universal and constitutes an unexplained human equation in diagnostic procedures; although it is disturbing to see the magnitude of disagreement in matters we might regard as more predictable, it is wise to perceive the degree of observer error in different fields. Johnson[12,13] suggests that we replace the security of thinking along well defined familiar channels by a new security based on acceptance of ambiguity, uncertainty and open chance. Maturity develops when we make our inevitable errors, identify and study them. Our objective is not to deny error but to learn from it.

CONCLUSION

A study of observer error and factors affecting it disclosed that 3 academic physicians had approximately the same degree of observer error in reading plain roentgenograms of the hands as did others in reported instances of similar studies over a considerable range of clinical medicine.

This study revealed:

1. That the set of comparator bones made no significant difference in the detection of osteoporosis, osteoarthritis and rheumatoid arthritis; although each observer felt more secure in his opinion when the comparator bone was used.

2. With pre-experiment agreement on roentgenologic signs identifying osteoporosis, osteoarthritis and rheumatoid arthritis, there were significant differences between readers when roentgenograms were read blindly.

3. Knowledge of diagnosis influenced all observers.

4. One reader noted 6 per cent positive

for osteoporosis; another read 14 per cent positive; and the third read 30 per cent positive. The incidence of osteoporosis was not significant in patients at bedrest, except as read by the one biased reader.

SUMMARY

A rheumatologist and 2 radiologists read 3 groups of 50 pairs of roentgenograms of patients' hands, one roentgenogram with and one without a comparator set of bones.

The categories were: Group I—normal subjects; Group II—surgical patients; and Group III—rheumatoid arthritis patients. They were matched for age and sex.

All readers had the same degree of observer error; comparator bones did not aid in the diagnosis of osteoporosis, rheumatoid arthritis or osteoarthritis; knowledge of the diagnosis influenced all observers' readings.

John H. Bland, M.D.
Rheumatology Unit
Department of Medicine
University of Vermont
College of Medicine
Burlington, Vermont 05401

REFERENCES

1. Belk, W. P., and Sunderman, F. W. Survey of accuracy of chemical analysis in clinical laboratories. *Am. J. Clin. Path.*, 1947, *17*, 853–861.
2. Birkelo, C. C., Chamberlain, W. E., Phelps, P. S., Schools, P. E., Zacks, D., and Yerushalmy, J. Tuberculosis case finding: comparison of effectiveness of various roentgenographic and photofluorographic methods. *J.A.M.A.*, 1947, *133*, 359–366.
3. Cochrane, A. L., and Garland, L. H. Observer error in interpretation of chest films: international investigation. *Lancet*, 1952, *2*, 505–509.
4. Cole, L. G. Pathological yardstick. *Surg., Gynec. & Obst.*, 1963, *63*, 689–716.
5. Cope, J. H., Harkness, J. T., Kennedy, B. R., and Yerushalmy, J. Role of dual reading in mass radiography. *Am. Rev. Tuberc.*, 1950, *61*, 443–464.
6. Davies, L. G. Observer variation in reports on electrocardiograms. *Proc. Brit. Cardiac Soc.*, (Abst.) *Brit. Heart J.*, 1956, *18*, 568.
7. Derryberry, M. Reliability of medical judgments on malnutrition. *Pub. Health Rep.*, 1938, *53*, 263–268.
8. Fletcher, C. M. Clinical diagnosis of pulmonary emphysema: experimental study. *Proc. Roy. Soc. Med.*, 1952, *45*, 577–584.
9. Garland, L. H. Clinical and laboratory observer variations. *J. New Drugs*, 1961, *1*, 65–71.
10. Garland, L. H. On scientific evaluation of diagnostic procedures. *Radiology*, 1949, *52*, 309–328.
11. Garland, L. H. Studies on accuracy of diagnostic procedures. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1959, *82*, 25–38.
12. Johnson, M. L. Observer error: its bearing on teaching. *Lancet*, 1955, *2*, 422–424.
13. Johnson, M. L. Seeing's believing. In: New Biology. Penguin Books, London, 1953, p. 60.
14. Paton, B. C. Accuracy of diagnosis of myocardial infarction: clinicopathologic study. *Am. J. Med.*, 1957, *23*, 761–768.
15. Tuddenham, W. J. Problems of perception in chest roentgenology: facts and fallacies. *Radiol. Clin. North America*, 1963, *1*, 277–289.

EPIPHYSEAL DYSOSTOSIS*

By HOWARD L. STEINBACH, M.D., *and* ROBERT A. BROWN, M.D.
SAN FRANCISCO, CALIFORNIA

RECENTLY we have examined 2 patients with skeletal deformities which in many respects were identical to those of diastrophic dwarfism, but the patients were not dwarfs and neither scoliosis nor dislocations of joints were present. Also, the pattern of autosomal recessive inheritance of diastrophic dwarfs did not prevail. We suggest that this entity be called epiphyseal dysostosis.

REPORT OF CASES

CASE 1. This 30 year old white man was hospitalized for evaluation of acquired rheumatic heart disease. Eventually, mitral and tricuspid valve prostheses were required. His height was approximately 5 feet, 6 inches and weight 130 pounds (Fig. 1, *A* and *B*). The predominant skeletal changes consisted of short extremities, particularly the forearms, and multiple deformities of the hands. No appreciable scoliosis was noted. The ears and palate were normal. In general, musculature was well developed and aside from the limitations imposed by the cardiac disease, the patient was active. The congenital anomalies had not resulted in any apparent physical limitations in his occupation as an agricultural worker. According to the history, the parents of the patient were normal (normal bone development of the mother confirmed by roentgenography). Five sisters and 3 brothers of the patient were in good health. There was no history of stillbirth or of early infant deaths in the family. A history of similar deformities of the hands in 4 of the 5 sisters was confirmed in 1 (Case II). All the sisters were 5 feet 3 inches, or more, in height. Of the 3 brothers, 2 were said to have similar hand deformities without other major skeletal anomalies. All were taller than 5 feet 7 inches. None of the siblings had had surgical procedures of cleft palate or talipes equinus. Most of the family could not be located and others were unwilling to submit to examination, which accounts for the lack of more detailed information.

The roentgenologic skeletal survey at the time of admission revealed the following:

Vertebral column (Fig. 2, *A* and *B*). A slight scoliosis appeared to be not significant. The contour of the end plates of multiple lower thoracic vertebrae was irregular. An anterior wedging of the eleventh and twelfth thoracic vertebral bodies produced a mild lower thoracic kyphosis. The interpediculate distances of the lumbar vertebrae were diminished and in the lateral view the pedicles of the fourth and fifth lumbar vertebrae appeared short.

Pelvis and hips (Fig. 3). The acetabula were shallow and increased in slope bilaterally. Although no dislocation was present, the heads of the femora protruded outside the acetabula and were somewhat bulbous.

Extremities (Fig. 4, *A* and *B*; 5; and 6, *A* and *B*). The heads of both radii were subluxated posteriorly and laterally and the joints between the ulnae and humeri were partially subluxated. The proximal ends of the ulnae were large and the size of the olecranon processes increased. An exostosis arose from the right humerus laterally near its central portion. The radii and the ulnae were unusually short compared to the size of the humeri. A Madelung's deformity was observed in each arm. The ulnae were displaced posteriorly at their distal portions and on the left, subluxation was also lateral. Compared with the underlying bone structures, the soft tissues of the hands appeared to be prominent. The second, third, and fifth middle phalanges and proximal first phalanges were extremely short. The adjacent articular surfaces of the second proximal phalanx and head of the second metacarpal sloped laterally. All of the metacarpals were short, but shortening of the first, third, fourth, and fifth was disproportionate, and the first metacarpal was almost square. The roentgenograms of the knees suggested a minimal coxa valga. Bilateral calcaneal and hammer-toe deformities were present. The metatarsals were short, particularly the first, and small exostotic growths arose from the medial aspect of both

* From the Department of Radiology, University of California School of Medicine, San Francisco, California.
Supported in part by USPHS Grant AM-02589.

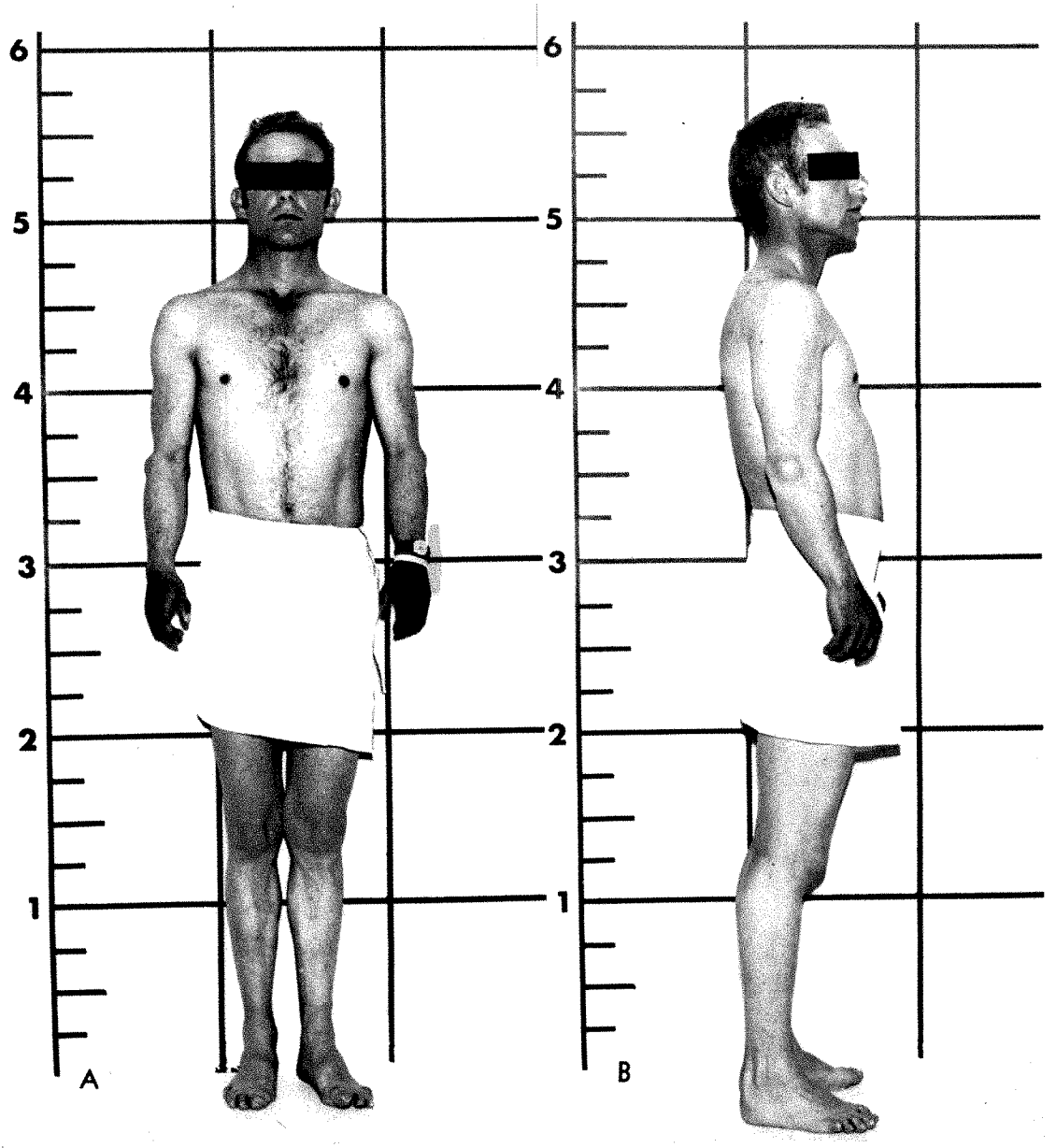


Fig. 1. Case 1. (*A* and *B*) Appearance at the time of roentgenologic examination. Lateral subluxation of the proximal radius is bilateral. The external ears are normal.

fifth metatarsals. On both sides the first, fourth, and fifth proximal phalanges were abnormally short.

The skull appeared normal.

Case II. This 30 year old married woman was the sister of Case 1. Aside from the hand deformities (Fig. 7, *A* and *B*), the clinical appearance was normal. According to the history, a 3 year old son was normal.

Skeletal survey roentgenograms were obtained and revealed the following:

Vertebral column (Fig. 8, *A* and *B*). The second and third cervical vertebral bodies and the posterior articulations were fused. The odontoid was not fused to the vertebral body. In the thoracic spine, the end plates of multiple vertebral bodies were irregular. Interpediculate distances of the lower lumbar spine were narrow.

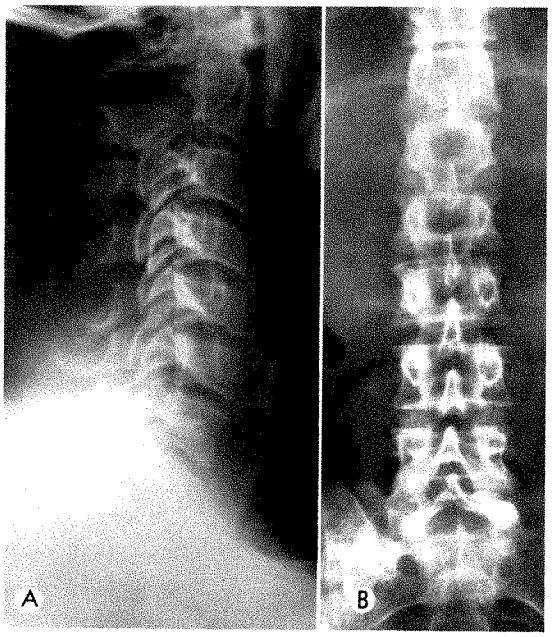


Fig. 2. Case 1. (*A*) The lateral view of the cervical spine shows flattening of the midcervical vertebral bodies and a gradual decrease in the anteroposterior diameter of the vertebral bodies inferiorly. (*B*) No significant scoliosis is seen in the lumbar spine. The interpediculate distances are narrow in the midlumbar and lower lumbar spine, instead of widening inferiorly as in the normal.



Fig. 3. Case 1. The acetabula are shallow and increased in slope. No dislocation is present but the heads of the femora protrude outside the acetabula and are somewhat bulbous.

Pelvis and hips (Fig. 9). The acetabula were somewhat shallow, from which bulbous femoral heads protruded slightly, as in the brother, but to a much lesser degree.

Extremities (Fig. 7, *A* and *B*). The elbows, forearms, and wrists appeared essentially normal. All of the metacarpals appeared short, the first, third, fourth, and fifth being disproportionately short. The first metacarpals were particularly short and somewhat expanded, forming an oblong. These changes were almost identical to those in the brother. One difference observed in this patient, however, was an extra center of ossification of the third

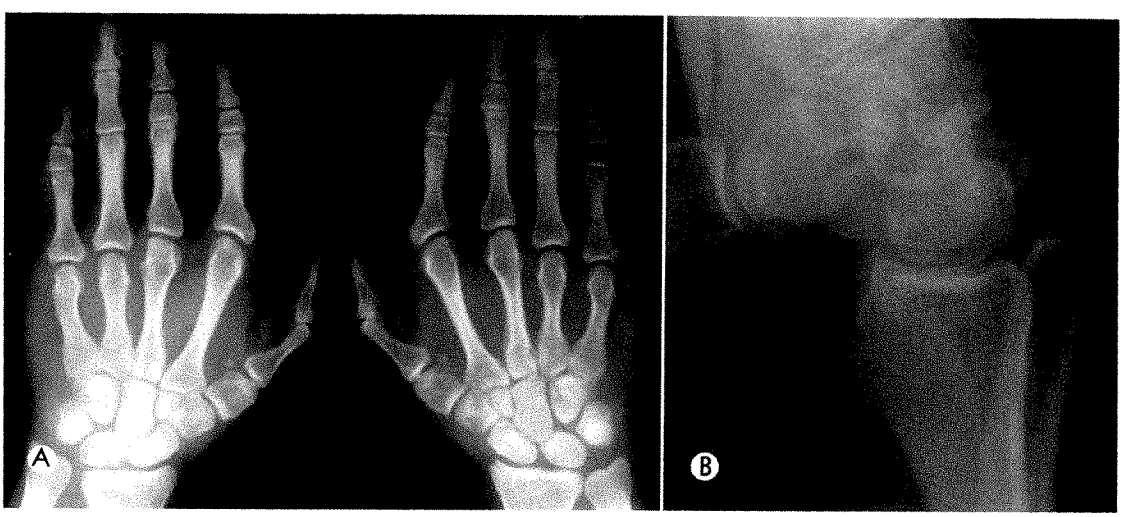


Fig. 4. Case 1. (*A*) All of the metacarpals are short with disproportionate shortness of the first, third, fourth, and fifth. The first metacarpal is almost square. The second, third, and fifth middle phalanges and proximal first phalanx are extremely short. The articular surface of the second metacarpophalangeal joints, bilaterally, slopes laterally. Madelung's deformity of the ulna is bilateral; on the left the ulna is subluxated laterally, as well. (*B*) The lateral view of the wrist shows posterior displacement of the distal ulna, bilaterally.



Fig. 5. Case I. The lateral view of the elbow shows that the proximal end of the ulna is large and the olecranon process is increased in size. The head of the radius is subluxated posteriorly and laterally

finger between the proximal phalanx and the metacarpal. This ossification probably represented an enlarged epiphysis that was not fused to the metaphysis of the proximal phalanx. Evidence of a large epiphyseal center that had been present at the base of the second

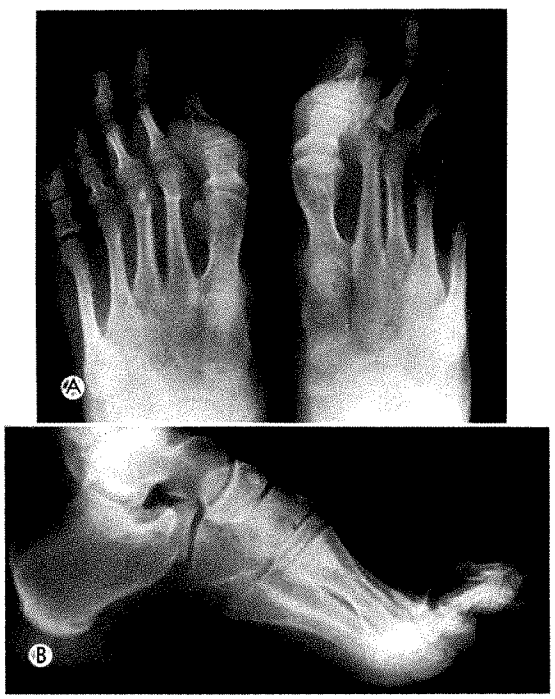


Fig. 6. Case I. (*A*) The metatarsals are short, particularly the first. The first, fourth, and fifth proximal phalanges are short, bilaterally. Small exostotic growths arise from the medial aspects of both fifth metatarsals. (*B*) Bilateral calcaneal and hammer-toe deformities were present.

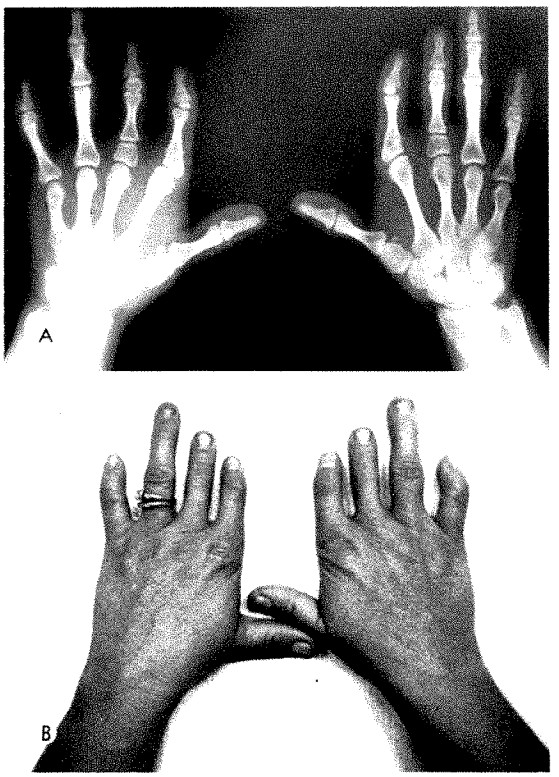


Fig. 7. Case II. (*A*) All of the metacarpals appear short with a disproportionate shortness of the first, third, fourth, and fifth. The first metacarpal is extremely short and somewhat expanded, forming an oblong or triangular shape. An extra center of ossification in the third finger between the proximal phalanx and metacarpal, probably represents an enlarged epiphysis that has not fused. A similar anomaly of the proximal phalanx of the second finger, however, is almost completely fused, bilaterally. The middle phalanges of the second, third, and fifth fingers are extremely short. The lateral sloping of the second metacarpophalangeal joint, bilaterally, is similar to that in the brother (Case I). (*B*) Photograph of the patient's hands for comparison.

proximal phalanx was also observed, but this was almost completely fused. The middle phalanges of the second, third, and fifth fingers of both hands were extremely short, as they were in the brother. A peculiar deformity of the second metacarpophalangeal joint was present on both sides, with angulation of the adjacent surfaces laterally. Roentgenograms of the feet were not obtained, but those of the ankles suggested a deformity similar to that of the brother.

The skull was normal.

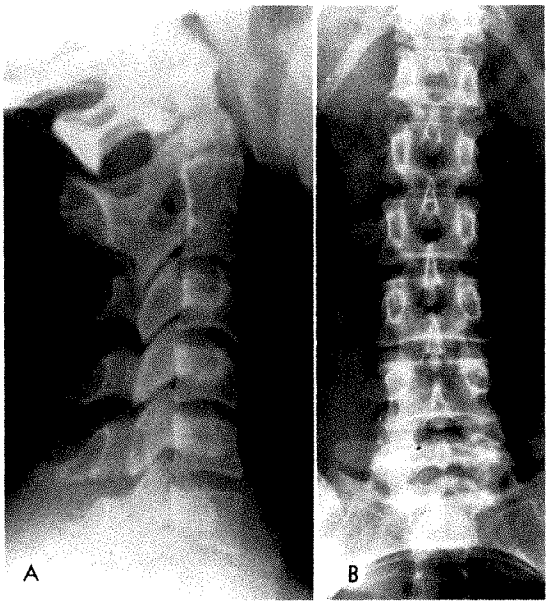


Fig. 8. Case II. (*A*) The lateral view of the cervical spine shows fusion of the second and third cervical vertebral bodies and posterior elements. The odontoid is not fused. (*B*) There is no significant scoliosis of the lumbar spine. The narrowing of the interpediculate distances in the lower lumbar level is similar to that seen in the brother (Case I).

For comparison we are presenting a case of diastrophic dwarfism, which may also be classified as a form of epiphyseal dysostosis.[7]

Case III. A male infant was referred to this institution at the age of 2 months for evaluation and treatment of multiple skeletal deformities. The child was a product of a normal full-term pregnancy and uneventful delivery. Both parents were normal. No family history of intermarriage or of congenital defects was known. Male and female siblings, $3\frac{1}{2}$ and 9 years of age, respectively, were normal. There had been no other pregnancies.

Except for the multiple skeletal deformities, the infant was a well-nourished active male, 56 cm. in length and weighing 6 kg. (Fig. 10). The hips and elbows were dislocated and bilateral talipes equinus and severe hand deformities were present. Motion was restricted at the elbows (limited extension) and wrists, and in most of the interphalangeal and metacarpophalangeal joints of the hands. The thumbs were freely movable. The external ears and palate were normal. No appreciable scoliosis was noted. Both patellae were absent. The diagnosis of arthrogryposis was considered and corrective treatment of the foot and hip deformities was begun. The equinus deformities of the feet proved to be refractory to treatment. Surgical correction of the dislocated hips was initially successful; however, the patient died of postoperative complications at the age of



Fig. 9. Case II. The acetabula are somewhat shallow with slight protrusion of the slightly bulbous femoral heads, similar to those of the brother (Fig. 3, Case I).

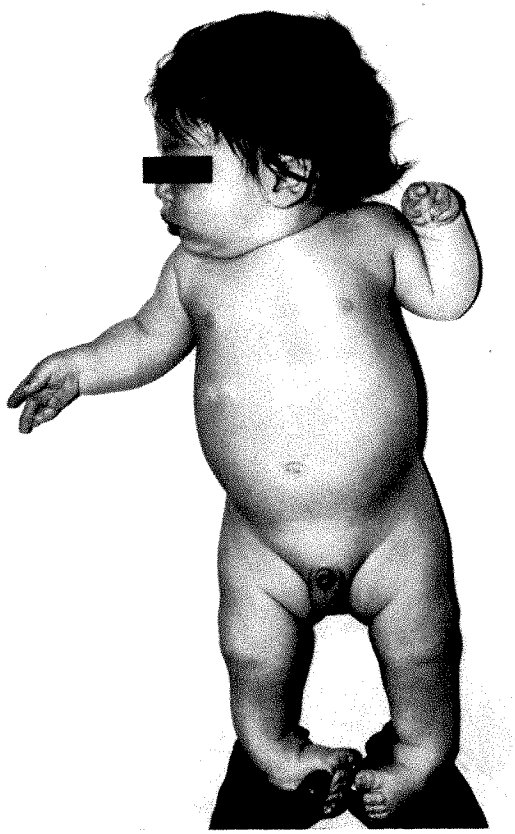


Fig. 10. Case III. Infant at $2\frac{1}{2}$ months of age.

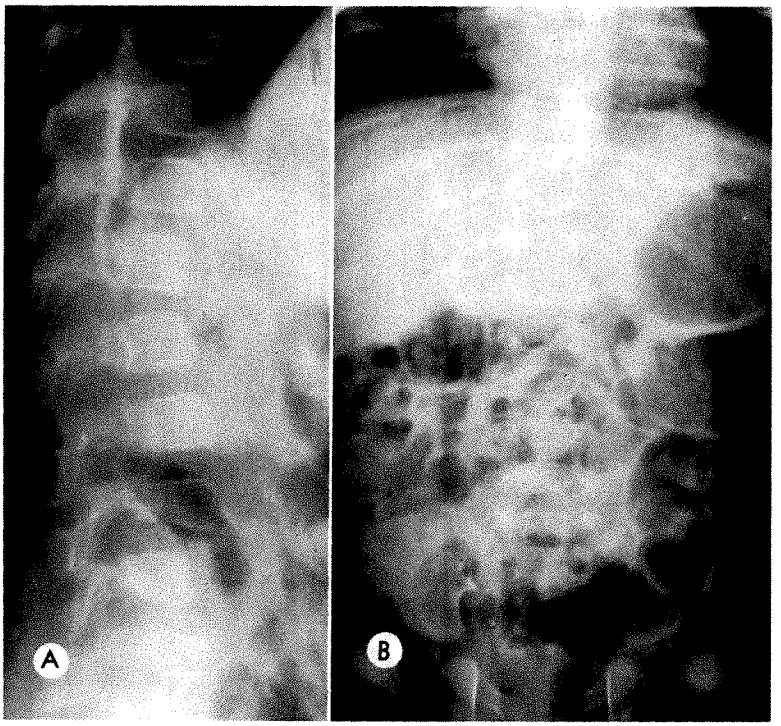


FIG. 11. Case III. (*A*) Lateral view of the spine shows that the body of the third lumbar vertebra is subluxated on the fourth lumbar vertebra. A slight kyphosis is present at the thoracolumbar junction. (*B*) Anteroposterior view of spine and pelvis. No appreciable scoliosis is present. The interpediculate distances of two midlumbar vertebrae are narrow with respect to those above and below, although absolute values are not decreased. Both hips are subluxated.

$3\frac{1}{2}$ years. Permission for necropsy could not be obtained.

A review of the patient's roentgenograms revealed the classic changes of diastrophic dwarfism.

Vertebral column (Fig. 11*A*). Subluxation was evident in the lower lumbar region with the third vertebra subluxated on the fourth. The interpediculate distances of the third and fourth lumbar vertebrae were narrow as compared with the vertebrae above.[1] The interpediculate distance widened normally at the fifth lumbar vertebra. In the lateral view, the length of the pedicles in the lower lumbar region appeared diminished. Scoliosis was not significant.

Pelvis and hips (Fig. 11*B*). Subluxation of both hips was present.

Extremities (Fig. 12; 13; and 14, *A–C*). The elbows were dislocated between the ulna and the humerus. A further subluxation was noted of the head of the radius with respect to the ulna. Bone maturation in the wrist was accelerated (the carpal bone age being that of a 3 year old), with one extra carpal center ossified at the age of 2 months. The first metacarpal was short and square. The middle phalanges were short, particularly the third, fourth, and fifth, and their bases were round rather than square. The space between the middle and proximal phalanx of the third finger was diminished, probably indicating absence of the epiphyseal center. The second proximal phalanx was short, its distal end being square rather than round. The proximal ends of the femora were somewhat expanded and externally rotated. Appearance of the distal femoral epiphyses was delayed; ossification was faint at 2 months of age. The proximal tibial epiphyses were large by comparison and were flat and mottled. The tibiae were subluxated medially with respect to the femora. The fibulae appeared disproportionately short with the metaphysis of the distal part being at about the same level as that of the tibiae. (Subsequent roentgenograms after development of the distal tibial epiphysis showed it to be flat and broad.) Roentgenograms of the feet showed equinovarus.



Fig. 12. Case III. The radius and ulna are subluxated posteriorly at the elbow. Further subluxation is seen at the head of the radius with respect to the ulna. Relative lengths of the radius and ulna are grossly normal.

DISCUSSION

Because of the marked similarity and distribution of skeletal lesions of our 2 patients to those of diastrophic dwarfs, a review of the skeletal lesions reported in such dwarfs is indicated. More than 20 cases have been reported, including both childhood and adult examples of the disease. In all patients reported to date, the skeletal manifestations have been severe and have imposed moderate to severe limitation on those afflicted.

The disease is apparently hereditary with autosomal recessive transmission and is usually recognizable at birth.

ROENTGEN FEATURES OF DIASTROPHIC DWARFISM[2–6,8–10]

Vertebral column. The vertebral bodies are frequently flat, fused or subluxated. Scoliosis and kyphosis are prominent features, although the scoliosis may not be apparent in the early disease. Narrowing of the interpediculate distances in the lumbar spine, as in achondroplasia, has been reported in several instances.

Pelvis. Superficially, the pelvis may re-



Fig. 13. Case III. The carpal bone age is advanced and an extracarpal center is densely ossified. The first metacarpal is short and square. The middle phalanges are short, particularly the third, fourth, and fifth. The space between the middle and proximal phalanges of the third finger is diminished, suggesting the absence of the epiphyseal center.

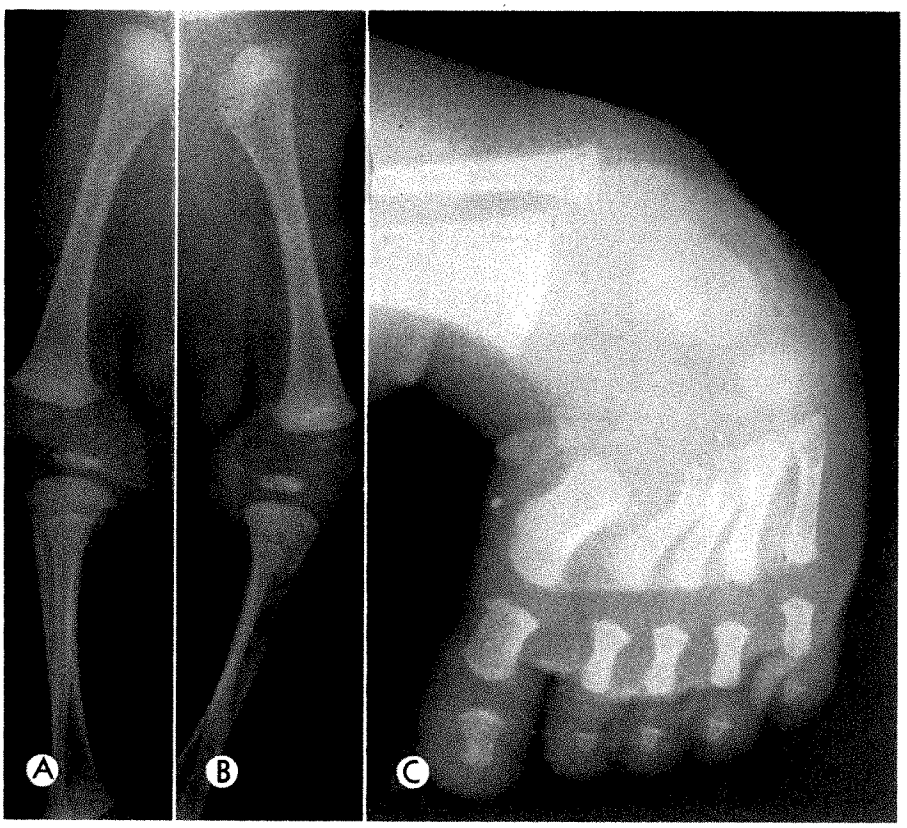


Fig. 14. Case III. (*A* and *B*) The appearance of the distal femoral epiphyses is delayed. They are faintly ossified at 2 months. The proximal tibial epiphyses are large by comparison and are flat and mottled. The tibiae are subluxated medially with respect to the femora. The fibulae appear disproportionately short. (*C*) An equinovarus is present. The first metatarsal is short and broad. The middle phalanges are underdeveloped.

semble that of achondroplasia, with a reduced angle of the acetabulum and flaring of the crests of the ilium. The sacrosciatic notch is not diminished, however.

Hips. The hips are frequently dislocated. The femoral heads may appear late with subsequent flattening and coxa vara.

Extremities. Micromelic (short-limbed) dwarfism is usually present and the distal portions of the extremities are usually shorter than the proximal. Frequently, the metaphyses are widened and the epiphyses are flat and wide. The epiphyseal centers are often delayed, except in the wrist where the converse is sometimes seen. Subluxations of the knee and elbow are frequent, particularly of the radio-ulnar joint, with which disproportionate shortening of the ulna is associated. The humeral heads may be enlarged and flattened and the glenoid fossa widened correspondingly. The proximal ends of the radius and ulna may be similarly enlarged with corresponding deformity of the distal humerus.

The wrists and hands are small. The carpal bones are frequently distorted and may appear prematurely, although, as noted above, maturation of the other epiphyseal centers is often delayed. The metacarpals are short, broad, and irregularly shaped and their length is frequently disproportionate. Many of the epiphyses are eccentric and asymmetric. The first metacarpal is usually extremely short and broad, sometimes being triangular in form. Considerable segmentation of the phalanges may be associated with disproportionate shortness. Some of the epiph-

yses may be unusually large, sometimes remaining as a separate center of ossification. In other instances they may be totally absent.

The appearance of the distal femoral epiphyses may be delayed. Frequently, flattening and deformity of the epiphyses may be associated with widening of the metaphyses of the distal femur. The degree of subluxation of the knees with medial displacement of the tibia and flattening of the tibial epiphysis has varied. The fibula may be disproportionately short in respect to the tibia.

Metatarsus varus and talipes equinus are frequent deformities. Metatarsal and phalangeal deformities are usually similar to those in the hands.

In some patients, cleft palate and characteristic external ear deformities have been reported. The skull is typically normal.

Diastrophic dwarfism has proved to be a distinct entity which can be diagnosed on roentgen examination. The term, "diastrophic," means tortuous or twisted. It referred to the marked scoliosis of the spine that ultimately developed in the original patients.[4] Dwarfism, of course, referred to the abnormally short stature. The first and second patients in this report are undoubtedly afflicted with a similar disorder, but to a milder degree. These two patients are not diastrophic, however, as scoliosis is not significant and stature is not pathologically short. The feature that would place them in the same category with diastrophic dwarfs is the malsegmentation of the hands and feet. Particularly, the very short first metacarpals and their square or oblong shape and the low-set thumbs are similar. The deformity of the feet in the first and second patients is not as severe as that reported previously in many patients with diastrophic dwarfism, or as in our Case III. Of particular interest is Case II, in whom the extra center of ossification in the middle finger of both hands was almost identical to that of the diastrophic dwarf of Case II of Stover, Hayes and Holt[9] and of Case II of Taybi.[10] Other similarities of our 3 patients to theirs were noted: shortness of the metacarpals, particularly the first; the peculiar deformity at the level of the second metacarpophalangeal joint; enlargement of the lateral aspect of the base of the proximal phalanx; and angulation of the head of the metacarpals. Also, in our Case I, the forearms were disproportionately short in comparison to the humeri. The increased acetabular angulation, the flattened cervical vertebrae, and the diminished interpediculate distance in the lower lumbar spine were similar to those changes described in other diastrophic dwarfs. In addition, in both patients (Cases I and II) Scheuermann's disease was evident, as it is in diastrophic dwarfism, and in Case II the second and third cervical vertebrae were fused. These 2 patients represent mild expressions of the same deformity as in our patient with diastrophic dwarfism and as in those reported in the literature under the term "diastrophic dwarfism."

Undoubtedly, additional patients similar to Cases I and II, or with other variants, will be described. The deformities described are primarily in the region of the epiphyses and, in all probability, they are secondary manifestations of defects in the supporting structures. A dysostosis has been described as a disturbance in ossification, such as that secondary to changes in soft tissues, muscles, or nerves. In these, the developmental defects are not always predictable.[7] We suggest that this disease be called "epiphyseal dysostosis without dwarfism." Diastrophic dwarfism can also be classified as a form of epiphyseal dysostosis but with dwarfism.

The epiphyseal dysostosis reported in Cases I and II was apparently present in 7 of 9 siblings but not in the parents. It would appear that the hereditary pattern differs from diastrophic dwarfism, which is rarely present in siblings.

SUMMARY

Two patients with a skeletal disorder resembling diastrophic dwarfism are reported. These patients are not dwarfs, how-

ever, and do not have scoliosis. The hereditary pattern also appears to differ from that of diastrophic dwarfism. It is proposed that these cases be classified as epiphyseal dysostosis.

Howard L. Steinbach, M.D.
Department of Radiology
University of California
San Francisco Medical Center
San Francisco, California 94122

REFERENCES

1. HAWORTH, J. B., and KEILLOR, G. W. Use of transparencies in evaluating width of spinal canal in infants, children, and adults. *Radiology*, 1962, *79*, 109–114.
2. JACKSON, W. P. U. Irregular, familial chondro-osseous defect; with suggestions concerning nomenclature of generalized osseous dystrophies. *J. Bone & Joint Surg.*, 1951, *33B*, 420–429.
3. KAPLAN, M., SAUVEGRAIN, J., HAYEM, F., DRAPEAU, P., MAUGEY, F., and BOULLE, J. Étude d'un nouveau cas de nanisme diastrophique. *Arch. franç. pédiat.*, 1961, *18*, 981–1001.
4. LAMY, M., and MAROTEAUX, P. Le nanisme diastrophique. *Presse méd.*, 1960, *68*, 1977–1980.
5. LANGER, L. O., JR. Diastrophic dwarfism in early infancy. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1965, *93*, 399–404.
6. MOTTA, C., and PIZZETTI, M. Su di un raro caso di osteochondrodistrofia dell'accrescimento con note acondroplastiche associato ad iperelasticita cutanea e lassita legamentosa. *Ortop. e. traumatol.*, 1958, *26*, 269–287.
7. RUBIN, P. Dynamic Classification of Bone Dysplasias. Year Book Medical Publishers, Inc., Chicago, 1964.
8. SILFVERSKIOLD, N. Sur la question de l'achondroplasie atypique et de sa forme périphérique. *Acta radiol.*, 1926, *5*, 223–235.
9. STOVER, C. N., HAYES, J. T., and HOLT, J. F. Diastrophic dwarfism. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1963, *89*, 914–922.
10. TAYBI, H. Diastrophic dwarfism. *Radiology*, 1963, *80*, 1–10.

USE OF A DIGITAL COMPUTER IN THE MEASUREMENT OF ROENTGENOGRAPHIC BONE DENSITY*

By FRED B. VOGT, M.D.,† LOUIS S. MEHARG, Ph.D.,‡
and PAULINE BEERY MACK, Ph.D.§
DENTON, TEXAS

THE optical density of a roentgenographic bone image can be related to the mass of bone material present if conditions of exposure and development of the film are standardized and kept constant. Marked departures from normal bone mineralization and changes in bone mass can be seen upon visual inspection of roentgenograms, but are not able to be quantitated without more refined techniques. It generally is recognized that changes in bone mineralization of the order of 25–30 per cent are necessary before visual inspection can detect changes in the roentgenogram. Changes of small percentage values in skeletal density, however, are of interest in many experimental and clinical situations. For example, the evaluation of drug therapy in disease processes such as osteoporosis and osteomalacia, as well as nutritional deficiencies, requires accurate techniques for determining serial measurements of skeletal density. Changes in bone mass in association with bed rest[5,8] and space flight[6] also require accurate and reproducible techniques.

In order to obtain quantitative measurements of the optical changes in a roentgenographic bone image, a controlled technique of exposure, film processing, and film analysis is required. In addition, a technique for calibrating the roentgenogram is essential. For the technique employed, an aluminum alloy wedge, the roentgenographic image of which is recorded simultaneously with the subject bone image, serves this purpose. A wedge used for the calibration standard in this laboratory has been made of an aluminum alloy selected to have x-ray absorption characteristics similar to that of the bone being analyzed. The alloy contains 93.4 per cent aluminum, 0.6 per cent manganese, 1.5 per cent magnesium, and 4.5 per cent copper. The light transmittance data from the wedge image are utilized subsequently to quantitate the light transmittance data from the bone image.

Using this technique, small changes in bone mass can be evaluated very accurately on serial roentgenograms of a human subject or an experimental animal. Somewhat less precise measurements are obtained when there are effects of such complicating factors as bone size changes (as occur in growth and maturation) and differences in absorption of the x-ray beam accountable to surrounding soft tissues. The selection of optimum exposure techniques, however, can reduce some of the differential effects from soft tissue and bone material. Such problems, which are inherent in a roentgenographic bone density technique, together with means of overcoming them, are described in other presentations.[1–4,6]

The purpose of this paper is to describe the application of a small digital computer to the analysis of data obtained from the output of an optical scanning system used to evaluate the light transmission through a roentgenogram. The system described is an updating and further automation of a bone densitometric assembly involving an analog system previously used at the Texas Woman's University.[1,5] Electromechanical calibrating and integrating techniques used

* From the Nelda Childers Stark Laboratory for Human Nutrition Research, Texas Woman's University, Denton, Texas.
† Affiliated with Texas Woman's University, Denton, Texas and The University of Texas Graduate School of Biomedical Sciences, Houston, Texas.
‡ Formerly associated with Kaman Instruments, Austin, Texas; now affiliated with The University of Texas Graduate School of Biomedical Sciences, Houston, Texas.
§ Director of the Texas Woman's University Research Institute, Denton, Texas.

in the older method for quantitative analysis of the roentgenographic image data have been replaced by the addition of a small digital computer.

DESCRIPTION OF THE NEW ASSEMBLY

For analysis of a roentgenographic image of a bone, it usually is desirable to have an integrated value for transmission of light over a line chosen on the roentgenogram. The light transmission data from the film, in the form of a voltage functional with per cent light transmission, are measured with a modified Knorr-Albers Microphotometer.* This is the same microphotometer as described previously,[1,5] except for the fact that the vacuum tube DC amplifier used in the unit has been replaced with a solid-state amplifier and power supply to provide the required stability. The film is held in a motor-driven assembly that traverses a light beam. The light beam at the film has a width of 10 microns along the scan path and a height of 1.25 mm. normal to the scan path. Nine scan speeds ranging from 0.1 cm./min. to 5.0 cm./min. are available. Adjustable limit-switches restrict the scan path to a predetermined range.

In Figures 1 and 2 a roentgenogram is shown with scan paths and microphotometer output voltages. Even though the original aluminum wedge is a linear function, the output is nonlinear. The wedge light transmission data are used to quantitate the bone light transmission data in terms of equivalent wedge thickness. In previously described systems, analog computer techniques employing adjustable function potentiometers were utilized to calibrate the light-transmission in terms of wedge-thickness for each film. Calibrated data from subsequent bone scans then were integrated by means of an electromechanical (Instron) integrator. These systems required that several step-by-step adjustments and calibrations be performed by an operator.

In the new assembly, the output of the scanning unit is connected through an amplifier (Astrodata Model 885) to a small digital computer (a Digital Equipment Computation PDP-8) as shown in the block diagram of Figure 3. A photograph of the system is shown in Figure 4. An analog-to-digital (A/D) converter formats the data for direct processing by the computer, and the computer samples the data at specific intervals of time. Programming and operating control is effected through a teletypewriter unit (TTY) that includes a paper-type input/output (I/O) feature.

The computer has been implemented to perform computations similar to the functions performed by previous analog systems. First, the wedge image is scanned and the resulting light transmission data are stored in terms of distance along (or thickness of) the wedge. Second, the bone image is scanned and the resulting light transmis-

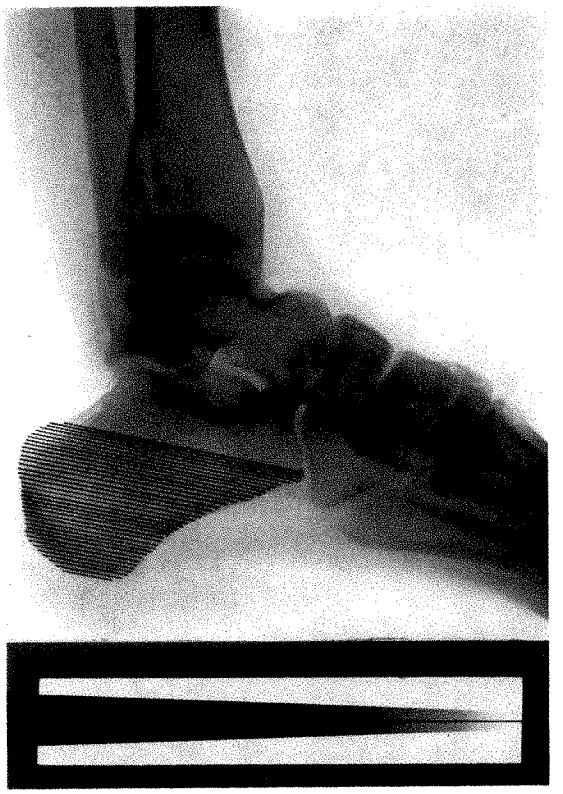


FIG. 1. Roentgenogram of human os calcis in lateral projection, with multiple scans covering approximately 60 per cent of the bone (upper) and of calibration wedge with central scan.

* Leeds and Northrup Company Catalog EM9-90(2)-1953, List No. 6700-Pl.

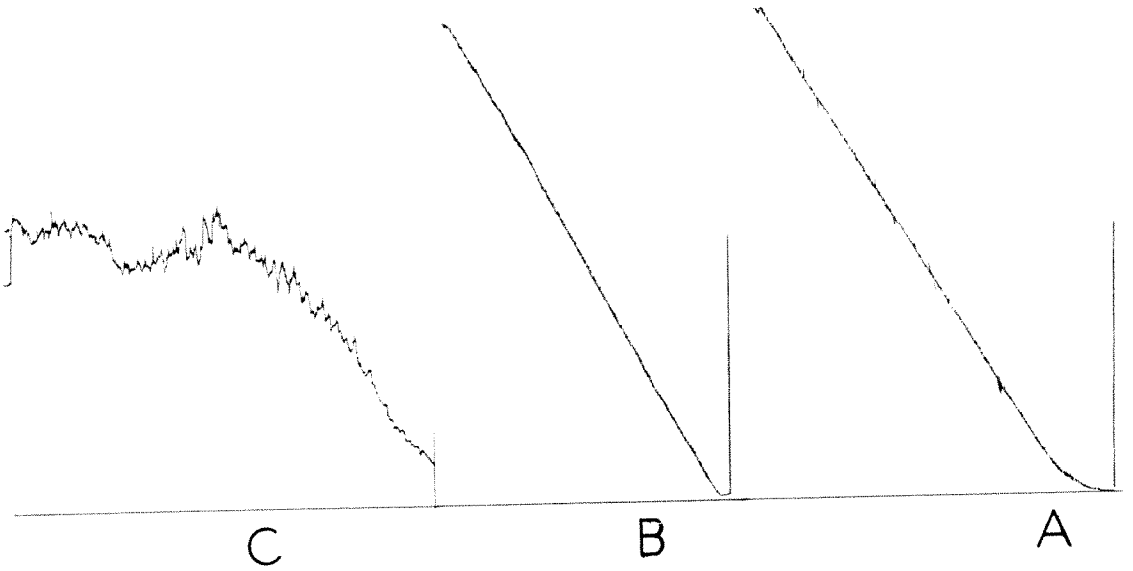


Fig. 2. Tracing of analog computer output for: (*A*) Initial calibration wedge scan; (*B*) corrected wedge scan; and (*C*) one of the scans across the os calcis roentgenogram.

sion data are stored. After both the wedge and bone scans have been completed, the computer calibrates the stored bone scan data in terms of equivalent wedge thickness by using the stored wedge scan data. The calibrated bone data then are integrated along the scan by using a trapezoidal approximation integration formula.

Because of the slow scanning speed and the low frequency components in the data, the system has been designed to provide a capacity for storage of 170 samples of the wedge scan data and 300 samples of bone scan data. The sampling rate has been established at 1 sample per second. For the standard wedge, scanned at 5.0 cm./min., 156 samples are produced in scanning from the beginning of the wedge to a point 13 cm. distant. The capacity of 300 samples of bone data allows scanning of bone lengths up to 25 cm. at a speed of 5.0 cm./min. Computation constants for the digital system were chosen to conform to the constants previously established for the analog system. Namely, the area under a wedge scan (scan of the wedge instead of a bone) is standardized as 6,500 units for a scan length of 13 cm. The integrator number for a bone scan can be converted to wedge thickness directly or to calcium hydroxyapatite equivalency for a unit volume of bone.

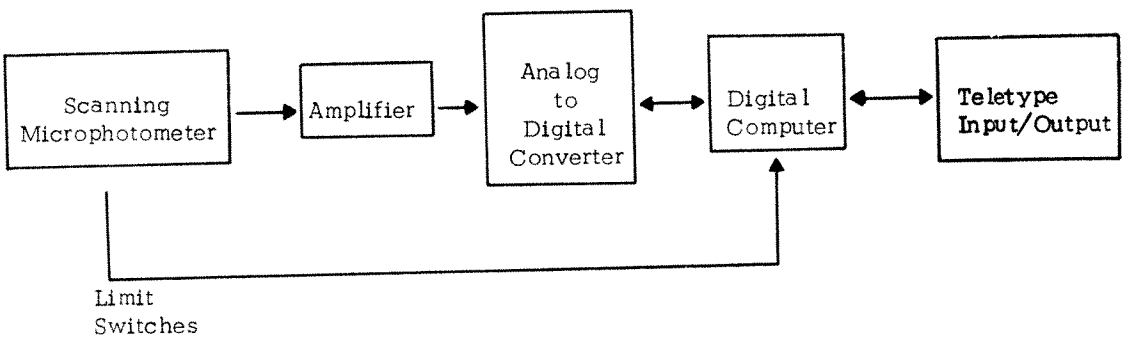


Fig. 3. Block diagram of microphotometer computer assembly.

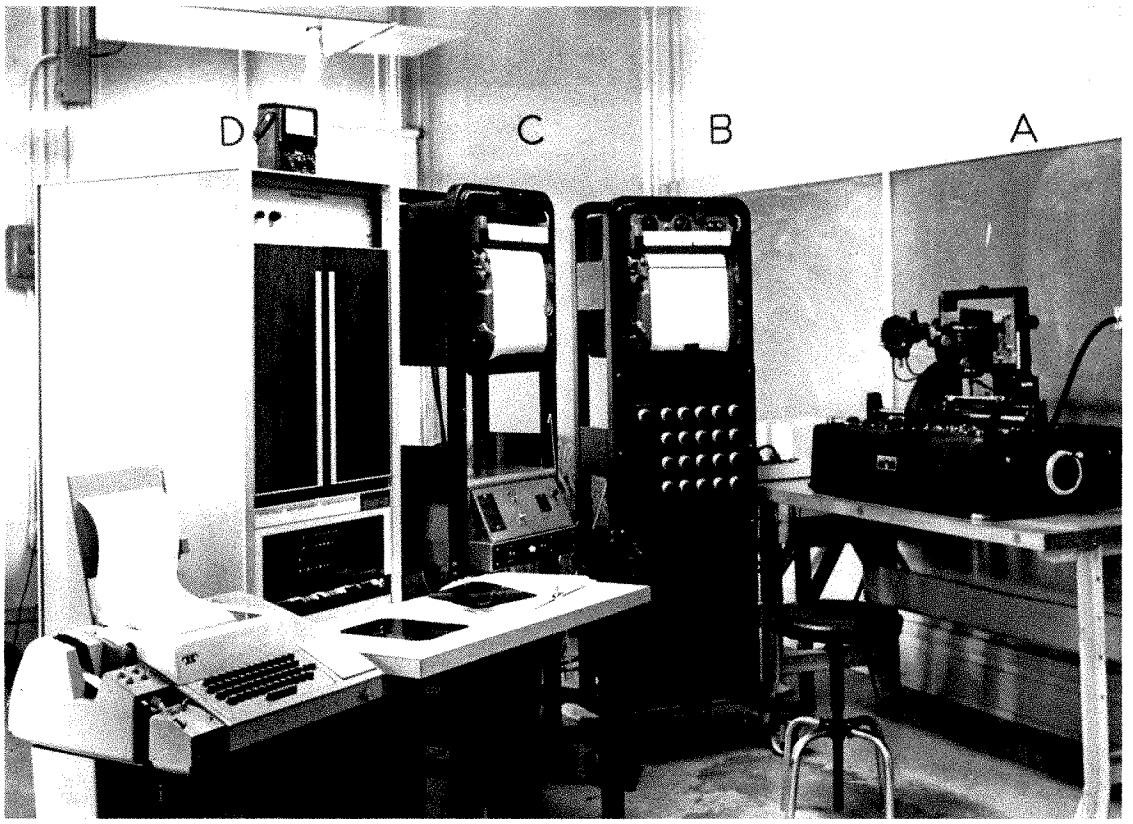


Fig. 4. Photograph showing the microphotometer and digital computer system. (*A*) Densitometer involving the analog system developed at the Texas Woman's University. (*B*) Transmitting recorder for tracing calibration wedge (upper), and potentiometers for correcting calibration wedge trace. (*C*) Recording potentiometer for scanning corrected wedge trace as well as the traces of bone scans. (*D*) Digital computer which has replaced the manual operations involved in *B* and *C* of the analog system.

In addition to the basic computational operations described previously, the computer program includes several operational features that permit flexibility in the use of the system. The teletypewriter input/output for a typical roentgenogram analysis is shown in Figure 5. After the system is activated, the computer prints *Waiting* (line 1). The operator inserts a control number to proceed with the heading information (proceed to line 3) *or* to skip the heading information (proceed to line 16). The heading information prior to the colons on each line are programmed into the computer. The operator types in the appropriate information after the colon. A *Carriage Return* initiates the next step. After the heading is finished (line 15), the computer prints *Wedge* (line 16). The operator initiates the scan sequence on the microphotometer. The limit switches control the data acquisition limits for the computer.

Subsequent to the wedge scan, the computer prints *Waiting* (line 17). Then the operator enters a control number directing the computer to print out the total area under the scan *or* the total area under the scan and the area of 10 equal-length segments under the scan. After this information is entered, the computer prints *Scan Speed* (line 19). The operator types the speed at which the bone will be scanned. (Note: the operator does not enter wedge scan speed; wedge scans are made at a speed of 5.0 cm./min. and this is programmed into the computer.) Upon the entering of *Scan Speed* by the operator, the computer will print *Bone* (line 20). The operator then

```
(1)     WAITING

(2)       9,9
(3)     SUBJECT NAME:
(4)     SUBJECT NUMBER:
(5)     EXPERIMENTAL UNIT:
(6)     DATE OF RADIOGRAPH:
(7)     DIET:

(8)     DATE OF SCANNING:
(9)     OPERATOR OF X-RAY MACHINE:
(10)    OPERATOR OF DENSITOMETER:

(11)    BONE:
(12)    BONE SITE:
(13)    TYPE OF WEDGE:
(14)    TYPE OF SCAN:
(15)    UNITS OF OUTPUT:


(16)    WEDGE

(17)    WAITING

(18)      Ø,-1

(19)    SCAN SPEED  5.Ø

(20)    BONE


(21)    NUMBER OF SAMPLE POINTS: +156
(22)    BONE LENGTH (CM): +Ø.13ØØØØE+2

(23)        SEGMENT       INTEGRATED COUNTS

(24)          +1             +Ø.564274E+2
(25)          +2             +Ø.2ØØ355E+3
(26)          +3             +Ø.332119E+3
(27)          +4             +Ø.467211E+3
(28)          +5             +Ø.598286E+3
(29)          +6             +Ø.731374E+3
(30)          +7             +Ø.8Ø5Ø87E+3
(31)          +8             +Ø.921Ø55E+3
(32)          +9             +Ø.1Ø3Ø56E+4
(33)          +1Ø            +Ø.114843E+4

(34)    TOTAL:               +Ø.629Ø86E+4        +Ø.3Ø8252E+1

(35)    WAITING
```

FIG. 5. Sample computer input/output for a roentgenogram analysis.

scans a bone image on the microphotometer. At the completion of the bone scan, the computer prints out lines 21 and 22, lines 23 through 33 if requested in line 18, line 34, and line 35.

This completes a single-scan analysis of a roentgenogram. If the operator desires to make a sequential scan on the same roentgenogram utilizing the same wedge data, then the proper control number inserted after the *Waiting* of line 35 will cycle the program to line 18 of the sequence. If a new roentgenogram is to be analyzed, then appropriate control numbers can cycle the program to line 1 *or* line 16 of the sequence.

DISCUSSION

The present system offers an advantage over the earlier system in providing an automatic means for calibrating the film in terms of the light transmission of the aluminum wedge, the roentgenogram of

which is taken simultaneously with the roentgenogram of the bone of interest. Earlier systems required several manual operations by the operator to analyze the film. In the new system, manual operations required of the operator have been reduced to those involving the scan of the film. The accuracy and reproducibility of the technique are limited primarily upon operator care in setting up the film for scanning, selection of the scan path, and precise adjustment of the scan limits to activate the start and stop of computation by the digital computer.

The previous system has been evaluated in considerable detail. The present technique also has been evaluated to show the reproducibility of successive scans. The results have been compared with the output of the analog system, with the finding that the analog and digital systems provide essentially the same results. The digital technique, however, offers a more rapid procedure for analyzing the films, and it also reduces the technical error that can be introduced by the operator.

Quantitation of bone mass changes in growing human subjects or experimental animals is more difficult than that in adults because of changes in the size of the bone. This problem can be solved with reasonable satisfaction by making a roentgenogram at right angles to the original film, with a correction applied for size of the x-ray image in the two dimensions. Bone mass per unit volume is determined for a section of bone 10 microns wide and the cross-sectional area in this manner.

The quantitative evaluation of bone density of human and animal bones depends upon the assumption that the photographic density of the image on the roentgenogram is related in a known manner to the mass of the bone upon which the roentgenogram is based. The values obtained from the integrator in the assembly can be computed in terms of calibration wedge mass equivalency as described by Mack, Vose and Nelson.[5] These results can be converted into calcium hydroxyapatite equivalency by application of a constant derived from the evaluation of a known quantity of $3Ca_3(PO_4)_2 \cdot Ca(OH)_2$ by this technique. If the term "calcium hydroxyapatite equivalency" is used, however, this does not denote that a specified number of grams of this mineral is present in the bone section evaluated. The term refers to the mass not only of the major mineral present, but also of the interstitial organic matter within the bone, and the over-and under-lying soft tissue which may be reflected in the roentgenogram. Conditions of exposure, including kilovoltage, milliamperage, and time have been selected which minimize the effect to soft tissues in comparison to the mineral components of the bone. Omnell[7] has shown, by using the exposure settings described by the authors that the ratio of soft tissue to bone is 1:4. This coincides with the finding in these laboratories that, under the conditions of exposure employed, the mass absorption characteristics of calcium hydroxyapatite and of the type of soft tissue which overlies and underlies the bones most frequently scanned have been measured as 0.70 and 0.17, respectively, with the soft tissue effect reduced further by the comparatively small thicknesses present in the scanning paths utilized.

CONCLUSION

This technique offers one of the most advanced approaches to the quantitative evaluation of x-ray density. It is most applicable, and is of the greatest use in studies requiring quantitative values on successive sections of bone which change little in size. For example, if the effect of a treatment of a patient is to be evaluated over a period of time, successive roentgenograms can be taken and evaluated. Basically, the same procedure can be applied in evaluating the effect on bone density after such conditions as prolonged bed rest, stress, or space flight.

Pauline Beery Mack, Ph.D.
Director, Texas Woman's University Research Institute
TWU Station, Box 3895
Denton, Texas 76204

The authors wish to acknowledge the assistance of Dr. Paul A. LaChance, former

member of the Biomedical Research Office of the National Aeronautics and Space Administration, Manned Spacecraft Center, Houston, Texas, who served as technical monitor of a contract to Kaman Instruments involving the attachment of the digital computer described in this report to the existing bone densitometry scanner at the Texas Woman's University. Acknowledgment also is due to Dr. Lawrence F. Dietlein, Assistant Director of Research, Manned Spacecraft Center of NASA, who sponsored the project of adding a Digital Computer to the Bone Densitometry Assembly at the Texas Woman's University. The work was supported under NASA Contract NAS 9–5880.

REFERENCES

1. Mack, P. B. Radiographic bone densitometry. Conference under sponsorship of the National Aeronautics and Space Administration and National Institutes of Health, NASA SP-64. Washington, D. C., March 25–27, 1965.
2. Mack, P. B., Brown, W. N., Jr., and Trapp, H. D. Quantitative evaluation of bone density. Am. J. Roentgenol. & Rad. Therapy, 1949, *61*, 808–825.
3. Mack, P. B., and LaChance, P. A. Effects of recumbency and space flight on bone density. *Am. J. Clin. Nutrit.*, 1967, *20*, 1194–1205.
4. Mack, P. B., O'Brien, A. T., Smith, J. M., and Bauman, A. W. Method for estimating degree of mineralization of bones from tracings of roentgenograms. *Science*, 1939, *89*, 467.
5. Mack, P. B., Vose, G. P., and Nelson, J. D. New development in equipment for roentgenographic measurement of bone density. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1959, *82*, 303–310.
6. Mack, P. B., LaChance, P. A., Vose, G. P., and Vogt, F. B. Bone demineralization of foot and hand of Gemini-Titan IV, V, and VII astronauts during orbital flight. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1967, *100*, 503–511.
7. Omnell, K. Quantitative roentgenologic studies on changes in mineral content of bone in vivo. *Acta radiol.*, 1957, Suppl. 148, 1–86.
8. Vogt, F. B., Mack, P. B., Beasley, W. G., Spencer, W. A., Cardus, D., and Valbonna, C. Effect of bed rest on various parameters of physiological function: Part XII. Effect of bed rest on bone mass and calcium balance. NASA Contractor report #182. National Aeronautics and Space Administration, Washington, D. C., 1965.

Vol. 105, No. 4

CONGENITAL ARTERIOVENOUS MALFORMATION OF THE FOOT*

By L. E. KELLERHOUSE, M.D., *and* K. RANNIGER, M.D.
CHICAGO, ILLINOIS

CONGENITAL arteriovenous fistulas of the extremities, although exceptionally rare, must be considered in cases of progressive, therapy resistant, skin necrosis localized to an extremity. Physical examination may reveal hemodynamic changes, but diagnosis of an arteriovenous shunt is confirmed by arteriography.[4,7,8,9]

The purpose of this communication is to present a case report of a massive arteriovenous fistula of the right foot which remained undiagnosed for 3 years.

REPORT OF A CASE

P. G. is a 14 year old Negro girl who was born with a small red macular lesion the size of a quarter on the plantar surface of the right foot. The patient developed normally and the lesion remained quiescent until the age of 11 years, when it ulcerated. The ulcer enlarged so rapidly during the next 3 years that the patient was unable to bear weight on her foot. On several occasions severe bleeding followed slight abrasive trauma to the skin of the foot. An attempt to debride the ulcer was unsuccessful.

On admission the patient was unable to walk and even the slightest pressure on her foot caused exquisite pain. The right foot was markedly swollen and numerous raised ulcers, many covered with a black ichor, eroded into the plantar surface of the foot. The musculature of the right leg was markedly atrophic, but there was no difference in the length of the legs. All arterial pulses were palpable and a Corrigan water hammer pulse was noted in the right femoral artery. The raised ulcers on the foot did not pulsate. A chest roentgenogram was normal. Roentgenograms of the right foot demonstrated marked demineralization of the bones and irregular soft tissue swelling surrounding the foot (Fig. 1). The skeletal dimensions of both feet and tibiae were identical. No soft tissue calcifications were evident.



FIG. 1. Marked demineralization and irregular soft tissue swelling are noted on roentgenogram of the foot.

A femoral arteriogram demonstrated increased caliber of the superficial femoral artery and of the popliteal artery and its three major branches. The arterial flow was markedly increased and visualization of the arteries of the foot occurred within 2 seconds after injection. From the enlarged posterior tibial and dorsalis pedis artery, multiple large tortuous vessels throughout the entire foot demonstrated massive early filling. These drained quickly into multiple vascular hamartomas which, in turn, filled multiple distended veins that ultimately emptied into the deep venous system of the

* From the Department of Radiology, University of Chicago School of Medicine, Chicago, Illinois.



Fig. 2. Femoral arteriogram shows massive arteriovenous shunt with simultaneous filling of arteries and veins.

right tibia (Fig. 2). No massive flow into the superficial venous system occurred. The arterial venous shunting was confined to the soft tissues. No true tumor vessels were demonstrated.

A below-the-knee amputation was performed, and multiple arteriovenous anastomoses between tortuous arteries and veins were seen—as demonstrated on arteriography. There was no bone involvement. The intercommunicating channels were composed of both artery and vein wall.

DISCUSSION

There are many causes of arteriovenous malformations, including congenital, neoplastic, traumatic, inflammatory, postsurgical, and degenerative vascular disease.[3,6] Congenital arteriovenous fistulas are usually found in the brain and lungs, and those of the extremities are extremely rare.[6] The history and findings in this patient are consistent with a congenital arteriovenous fistula. Although the skin abnormality was detected at birth, it remained dormant for many years before ulcerating. This history is not unusual. Patients have been reported who were born with small cavernous hemangiomas on their extremities that later developed into massive arteriovenous shunts,[3,7,8] although degeneration of a hemangioma usually follows trauma or inflammation.[1] Massive shunts are also reported to arise *de novo* following infection or trauma.[3] Venous and arterial insufficiency—frequent cause of multiple solitary arteriovenous fistulas[5]—was not present.

Local hypertrophy secondary to an arteriovenous fistula of an extremity occurs in 60–80 per cent of patients.[3,8] Such hypertrophy usually occurs when the fistula shunts significantly during an active growth period. However, if the fistula enlarges after a major growth period, hypertrophy may not occur. In our case the arteriovenous malformation did not become active until after the patient was 11 years of age. Since most of her growth had occurred by this age, we feel that there was little opportunity for hypertrophy to occur. Marked demineralization of the skeleton of the leg and muscular atrophy are probably due to disuse in this case, rather than secondary to arteriovenous shunting. High output failure with cardiomegaly, frequently reported in patients with congenital arteriovenous fistulas of the extremities,[7,8] was not present in our patient.

Klaus Ranniger, M.D.
Department of Radiology
University of Chicago
950 East 59th Street
Chicago, Illinois 60637

REFERENCES

1. Cary, F. Fistules artério veineuses congénitales. *Mém. Acad. chir.*, 1953, 79, 152–159.
2. Coursley, G., Ivins, J. C., and Barker, N. W.

Congenital arteriovenous fistulas in extremities: analysis of 69 cases. *Angiology*, 1956, *7*, 201–217.

3. CURTIS, R. M. Congenital arteriovenous fistulae of hand. *J. Bone & Joint Surg.*, 1953, *35A*, 917–928.
4. GOIDANICH, I. F., and CAMPANACCI, M. Vascular hamartomata and infantile angioectatic osteohyperplasia of extremities. *J. Bone & Joint Surg.*, 1962, *44A*, 815–842.
5. HAIMOVICI, H., STEINMAN, C., and CAPLAN, L. H. Angiographic evaluation of arteriovenous shunting in peripheral vascular diseases. *Radiology*, 1966, *87*, 696–704.
6. KITTREDGE, R. D., KANICK, V., and FINBY, N. Arteriovenous fistulas. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1967, *100*, 431–445.
7. MALAN, E., and PUGLIONISI, A. Congenital angiodysplasias of extremities. *J. Cardiovasc. Surg.*, 1964, *5*, 87–130.
8. MALAN, E., and PUGLIONISI, A. Congenital angiodysplasias of extremities. *J. Cardiovasc. Surg.*, 1965, *6*, 255–345.
9. MURPHY, T. O., and MARGULIS, A. R. Roentgenographic manifestations of congenital peripheral arteriovenous communications. *Radiology*, 1956, *67*, 26–33.

MAMMOGRAPHIC TECHNIQUE: NEED FOR ROUTINE SPOT ROENTGENOGRAMS

By M. B. HERMEL, M.D.,* J. GERSHON-COHEN, M.D., D.Sc. (MED.),†
and R. N. BYRNE, M.D.‡
PHILADELPHIA and WEST CHESTER, PENNSYLVANIA

THE radiologist who does mammography cannot make a sound diagnosis of pathology unless he has the evidence on the roentgenograms. Much has been written in the literature about proper mammographic techniques to obtain roentgenograms with good quality and contrast.[1,3,6] The necessity of obtaining projections of the entire breast is also stressed: usually 2 routine projections, the cephalocaudad and the mediolateral, are said to suffice.

At times, however, these projections will disclose nothing. The patient, despite her localization of symptoms, is dismissed as being healthy, only to return later with advanced pathology. In actuality, her lesion has been overlooked because special projections were omitted. Spot roentgenograms should be taken of any area where symptoms or signs are localized.

In order to make certain of this necessity, we first do a careful physical examination. If a palpable mass is present, or if symptoms can be localized, we place a lead BB shot on the skin over the site with Scotch tape. This marker is easily identified on the roentgenograms. We then use the projection or projections that place the suspect area closest to the film, compressing the breast to do so. Such special projections often show lesions that routine roentgenograms have missed, as is demonstrated in the following illustrative cases.

REPORT OF CASES

CASE I. B. B., aged 50 years, complained of a drawing sensation in the upper outer quadrant of the right breast. Physical examination revealed small, compact breasts in which bilateral multinodularity was present. No specially dominant mass was palpable in the area of which the patient complained, and so a localized opaque marker was not placed over the area of complaint. When the mammographic examination was done, using cephalocaudad and mediolateral projections, nothing abnormal was seen.

The patient was recalled and a BB marker was placed over the area of symptoms. It was immediately noted on the roentgenograms that beneath the skin marker there was an area of localized edema involving the skin, which was thickened. Beneath the marker the trabecular pattern was distorted, as is seen with infiltrating ductal carcinoma (Fig. 1, *a* and *b*). A diagnosis of cancer was made on the basis of these findings, and was confirmed by histopathologic studies, which revealed a duct cell cancer. Examination of 18 axillary lymph nodes showed no evidence of metastatic spread.

The surgeon in this case was a long-time adherent of mammographic examination, and we had no difficulty persuading him to operate despite the absence of positive clinical findings.

CASE II. C. C. H., aged 56 years, reported to her physician for examination immediately after she inadvertently found a lump in her right breast. Physical examination revealed a palpable mass about 2.5 cm. in diameter occupying the upper lateral margin of this breast.

Cephalocaudad and lateral projections showed nothing, much to the surprise of the radiologist. A skin marker on the area had been omitted in the belief there would be no difficulty in demonstrating such an obvious tumor. The patient was recalled, and this time the precaution was taken to place a skin marker over the mass. Spot roentgenograms were then taken. These revealed portions of the mass, which was difficult to project fully because of its location close to the lateral chest wall.

The portions seen beneath the skin marker

* Assistant Professor of Radiology, Jefferson Medical College and Hospital, Philadelphia, Pennsylvania.
† Professor of Radiologic Research, Temple University School of Medicine, Philadelphia, Pennsylvania.
‡ Chief, Department of Radiology, Chester County Hospital, West Chester, Pennsylvania.

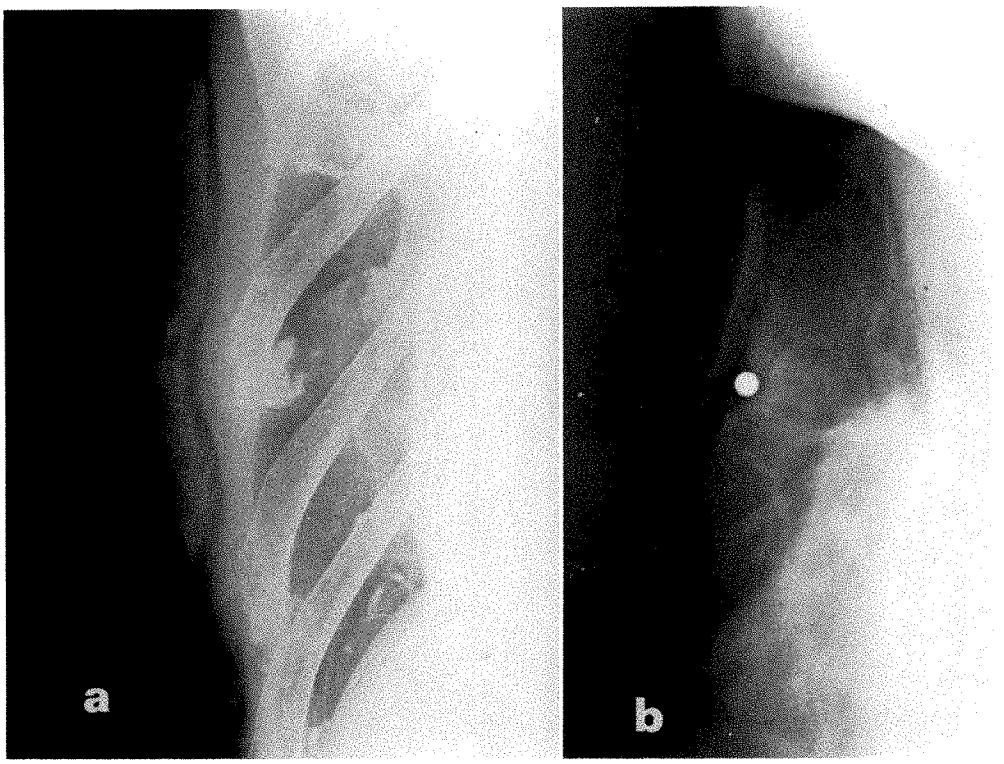


Fig. 1. Case I. (*a*) Lateral view of right breast without a localizing skin marker over the area of complaint. Nothing abnormal was seen or palpated. (*b*) Re-examination after placement of skin marker over area of symptoms reveals a small, spiculated mass and perifocal edema involving localized area of skin. This was not appreciated clinically. A duct cell cancer was found at operation, which was suggested by the roentgenologist in spite of the absence of clinical suspicion.

disclosed an undulating margin, with fine striae streaming out into the perifocal tissue. The details of the tumor were blurred because perifocal edema was present (Fig. 2, *a* and *b*).

With these signs at his command, the radiologist made the diagnosis of a malignant process without hesitation. Operation followed, and histopathologic study revealed the presence of a lymphosarcoma.

Case III. M. C., aged 49 years, had a palpable mass in the left breast, which the surgeon suspected to be cancer. Roentgenograms in routine cephalocaudad and lateral projections were made after a BB shot had been placed to identify the mass. In these routine studies, however, the skin marker was not visible due to faulty angulation, although the spot roentgenograms brought two-thirds of the mass into view (Fig. 3). It was difficult to visualize the entire mass because it was very close to the chest wall, near the upper outer margin of the breast. The film was placed so that the central roentgen ray projected cephalad from below.

The unevenness of the margins of the tumor, as disclosed by the spot roentgenograms, furnished confirmatory evidence of a cancer. The findings helped materially to reconcile the patient's willingness to undergo surgery without delay. A duct cell carcinoma was found.

DISCUSSION

We have long made a practice of taking spot roentgenograms of areas of breast complaints, although there are those who feel that such special projections are superfluous and add nothing to diagnosis.[6] Many patients have scars from previous breast operations done to establish a diagnosis. In these cases, it is our custom to attach a row of small BB shots over the linear scar (Fig. 4). Such skin marking does not interfere in the slightest with interpretation. It is, in-

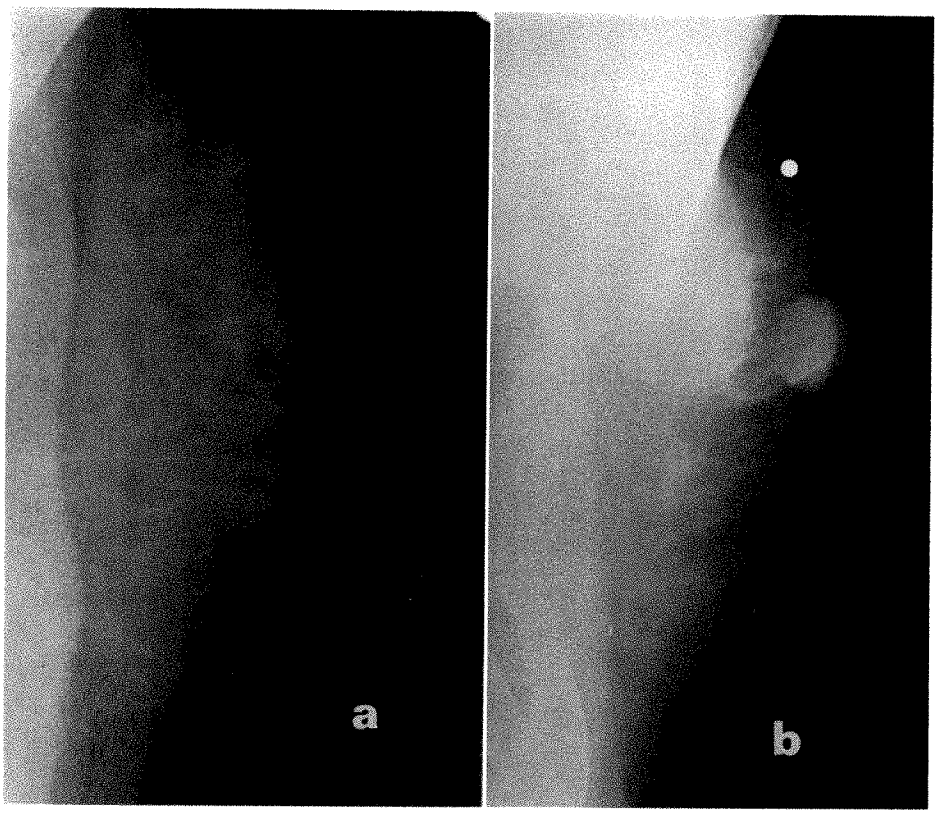


Fig. 2. Case II. (*a*) A mass about 2.5 cm. in diameter was palpable in the right breast. No skin marker was placed for orientation because the radiologist expected its presence to be clearly discerned on the roentgenogram. To his surprise, this was not the case in either the lateral or cephalocaudad views. (*b*) After placing a skin marker, a special compression film was obtained and a mass was seen. The undulating edges and the fine striae streaming into the perifocal tissues led to a presumptive diagnosis of cancer. The histologist found a lymphosarcoma.

deed, of great assistance, explaining structural distortions as being due to prior surgery rather than to some new pathologic infiltrative process.

It was encouraging to read in recent literature that Minagi *et al.*[5] agree that spot roentgenograms are important. They also add that they find compression coning of value, and this reasoning, too, affirms our long-felt convictions.[2] Compression reduces the object-to-film distance; tends to immobilize the breast tissue more completely; may displace superimposed glandular and fibrous tissue from the area under study, thus affording better evaluation of the lesion; and, because of the subsequent reduction in kilovoltage, promotes increased contrast and improved detail. Lasky[4] also espouses breast compression and recently described an improved technique to achieve it.

We believe it is important that the x-ray beam *traverse the lesion* if the area of concern is to be projected properly. The site of the lesion can always be confirmed by the skin marker. When radiologists and technicians alike appreciate the necessity for this precision, maintaining at the same time high standards of contrast, optimal delineation of detail, and meticulous processing of the films, mammography approaches its diagnostic zenith.

Considering the unique role that mammography is privileged to play in the detection of breast cancer, no radiologist can afford to be less than thorough. Spot

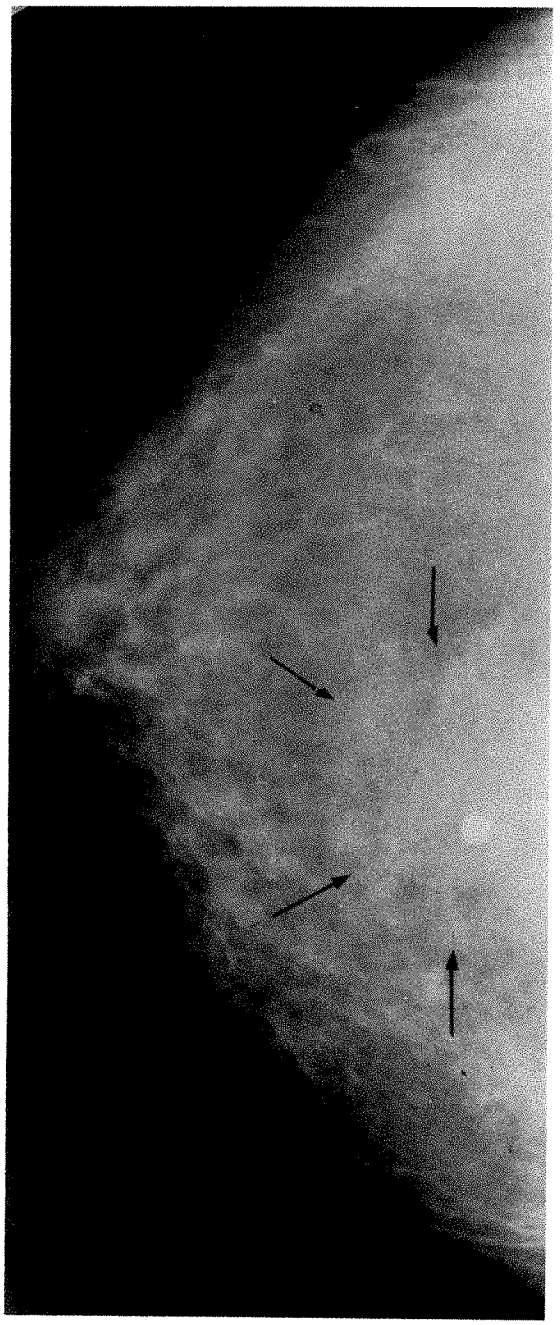


Fig. 3. Case III. A palpable mass in the upper outer quadrant of the left breast, identified with an overlying skin marker, was best demonstrated by a spot roentgenogram placed close to the lesion, with the central ray projected from below in a cephalad direction. The density of the mass is so similar to that of the surrounding tissues that its presence was made more easily visible by the skin marker.

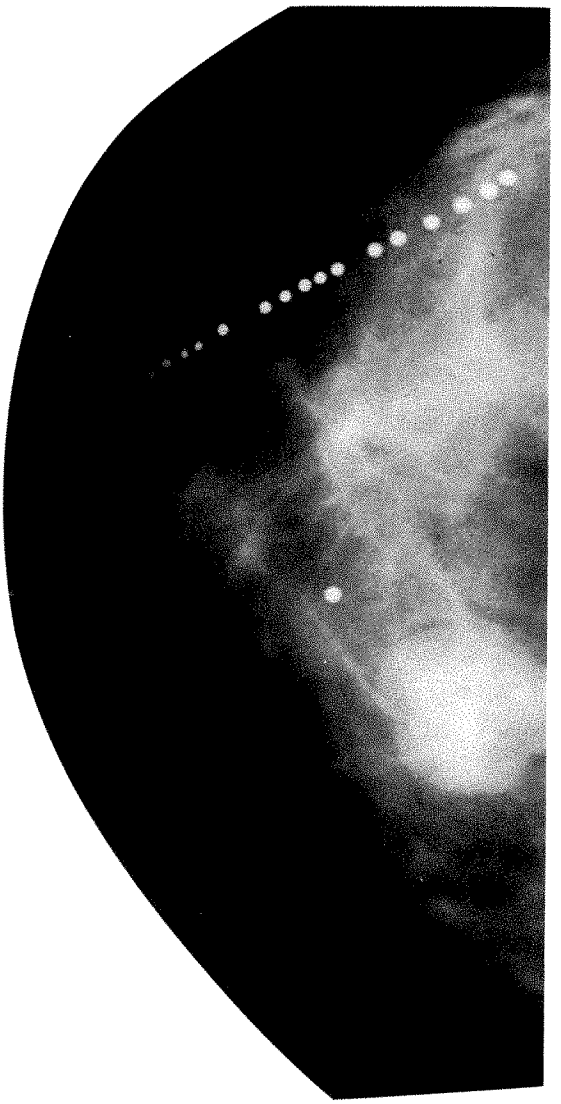


Fig. 4. Two rows of BB shots have been placed over the scars of two previous operations, so that the distortion of the underlying structural pattern is explainable. The single skin marker was placed over an isolated, palpable tumor. Even though it resembled a benign, smoothly-contoured lesion and was reported as a cyst by the histologist, its removal was recommended since a scirrhous or medullary cancer can have a similar notched, smoothly-contoured appearance.

roentgenograms and compression coning are integral parts of this thoroughness. These techniques should never be regarded casually if any patient's breast symptoms have not been explained by routine views.

SUMMARY AND CONCLUSIONS

Routine mammograms will often fail to demonstrate pathology, as is illustrated in 3 cases which accompany this report.

Special spot roentgenograms and compression coning should be mandatory procedures in any patient who has symptoms.

It is also wise to mark the area of concern so that it can be clearly identified on the roentgenograms, and to be certain that the projections disclose this marker.

J. Gershon-Cohen, M.D.
255 S. 17th Street
Philadelphia, Pennsylvania 19103

REFERENCES

1. EGAN, R. L. Mammography. Charles C Thomas, Publisher, Springfield, Ill., 1964.
2. GERSHON-COHEN, J., BERGER, S. M., CURCIO, B. M., and DELPINO, L. Mammography: some remarks on techniques. *Radiol. Clin. North America*, 1965, *3*, 389–401.
3. GROS, C. M. Les maladies du sein. Masson et Cie, Paris, 1963.
4. LASKY, H. J. New mammographic technic. *Radiology*, 1968, *91*, 381–383.
5. MINAGI, H., TENNANT, J. C., and YOUKER, J. E. Coning and breast compression: aid in mammographic diagnosis. *Radiology*, 1968, *91*, 379–381.
6. WOLFE, J. N. Mammography. Charles C Thomas, Publisher, Springfield, Ill., 1967.

VOL. 105, NO. 4

THE USE OF HYSTEROGRAPHY IN THE DETECTION OF HYDATIDIFORM MOLE*

By EDWARD I. GREENBAUM, M.D.,† G. PODOLAK, M.D.,‡ *and* B. J. O'LOUGHLIN, PH.D., M.D.§
IRVINE, CALIFORNIA

HYDATIDIFORM mole has been defined as a proliferation and cystic degeneration of young chorionic villi. Embryologically, the chorion develops from the trophoblast which invades the endometrium and, by the 14th day of gestation, erodes the stroma and capillaries. The chorionic villi formed are thus bathed in maternal blood which forms the beginning of the placental sinuses.[4] By the 18th day the primitive vessels appear and thereby vascularize the villi. The pathogenesis of the hydatidiform mole begins at the time when the whole of the chorion is villous before the formation of the placenta. There is a cystic, hydropic swelling of the chorionic villi, and eventually these fill the uterine cavity with a delicate, friable mass of thin-walled, translucent cystic and grape-like structures that rupture easily and collapse with the release of clear fluid. These grape-like clusters are held together by delicate fibrous strands. The fetus and amniotic cavity do not develop.[12]

CLINICAL FINDINGS

Hydatidiform mole appears in approximately 1 of 2,000 pregnancies. Bleeding may occur early, but in approximately 75 per cent of patients, passage of molar tissue does not occur prior to 12 weeks, and in over 50 per cent of cases, no molar tissue is passed until after 20 weeks of gestation. The uterus is larger than would be expected from menstrual dates in 50 per cent of the cases; however, in 25 per cent of the cases it is smaller, and in the remainder of the cases the size corresponds to the period of gestation. The fetus does not develop and therefore cannot be ballotted. There is no fetal movement noted by the mother, *i.e.*, quickening; and no heart tones can be heard by the physician. Signs of preeclamptic toxemia occur in up to 40 per cent of cases, and when this condition appears it is noted much earlier than is usual in a pregnancy accompanied by a fetus.[6] Although it is well known that urinary chorionic gonadotropin levels are increased in this condition, there still may be confusion between 10 to 14 weeks as there is often overlap with those values found in normal pregnancy.[18] Amniography is thus indicated in questionable cases of hydatidiform mole in the earlier stages of gestation, at which time there is no history of passage of molar tissue, no fetal skeleton is visualized on the roentgenograms, and the HCG levels are equivocal.

TECHNIQUE

Patients selected for hysterography are brought to the X-ray Department where they are first asked to either void or a catheter is placed to empty the bladder. A preliminary roentgenogram of the abdomen is taken in the anteroposterior projection. The patient is then surgically prepared and draped. A point approximately 3–5 cm. below the umbilicus in the midline is selected and 5 to 10 cc. of 1 per cent Xylocaine is infiltrated down to the peritoneum. A No. 18 spinal needle is then introduced transabdominally into the uterine cavity so that the needle tip lies in the intervesicular space. Twenty to 30 cc. of hypaque is introduced and immediately an anteroposterior roentgenogram is taken.

* From the Department of Radiological Sciences, The University of California College of Medicine, Irvine, California.
† Clinical Instructor, Radiological Sciences, U. C. Irvine.
‡ Formerly: Chief Resident, Obstetrics-Gynecology, Orange County Medical Center, Orange, Calif., now engaged in private practice.
§ Chairman and Professor, Radiological Sciences, U. C. Irvine.

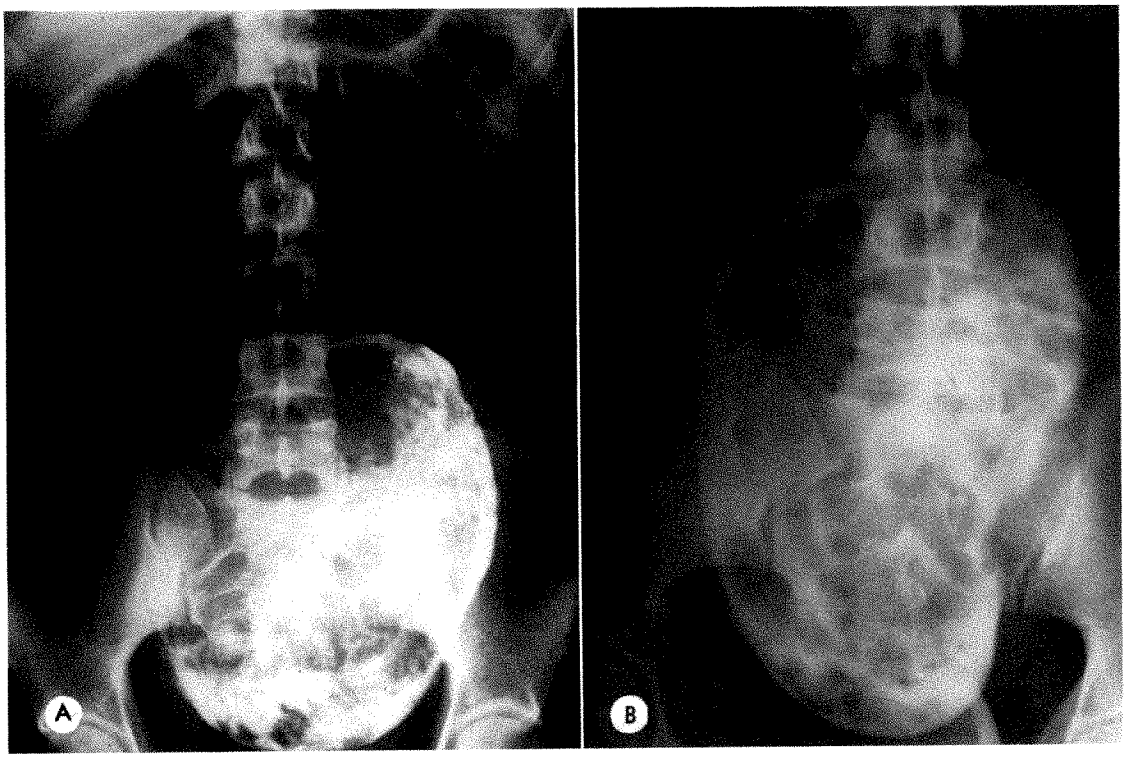


Fig. 1. Case I. (*A*) Anteroposterior and (*B*) oblique hysterograms reveal enlarged uterus with typical moth-eaten appearance of hydatidiform mole.

If this corroborates the diagnosis of hydatidiform mole, a lateral and an oblique roentgenogram are added. We first examine the anteroposterior roentgenogram in an attempt to reduce the radiation hazard posed by the additional two views in the event a normal fetus is present. If a mole is seen, the additional roentgenograms are taken within 5–10 minutes as the contrast medium is rapidly absorbed by the hypervascular gravid uterus.

REPORT OF CASES

Case I. A 23 year old Mexican American female, gravida IV, para II, ab. I, was admitted on March 26, 1968. Her last menstrual period was on September 6, 1967. She gave a history of vaginal bleeding for the past 2 months and, on examination, the uterus was smaller than would be expected with the stated gestational age. The patient noted no fetal movements and the physician was unable to hear the fetal heart tones or ballotte a fetus. The fetal electrocardiogram was negative and the urinary chorionic gonadotropin titers were elevated. A flat roentgenogram of the abdomen showed no fetal skeleton. Amniography was then done by the above technique and revealed the typical "moth-eaten" appearance of a hydatidiform mole (Fig. 1, *A* and *B*). The patient was started on a pitocin drip and expelled the mole in its entirety. A dilatation and curettage was then done. Following this, the patient has noted no vaginal bleeding, the uterus has involuted normally, and HCG levels have returned to normal titer. Follow-up will be continued over the next 2 years.

Case II. A 19 year old white American female was admitted on March 23, 1967. Her last normal menstrual period was on November 12, 1966, and it was felt that she was approximately by menstrual dates at 16 weeks of gestation. The patient stated that she had done well until January 1967, when she noted onset of a bloody vaginal discharge, but noted no passage of "grapes." On the day of admission she began to have cramping lower abdominal pains associated with a marked increase in the amount of vaginal bleeding. On physical examination, the blood pressure was 150/100 and the patient was noted to have generalized edema involving her face, feet and hands. The height of her

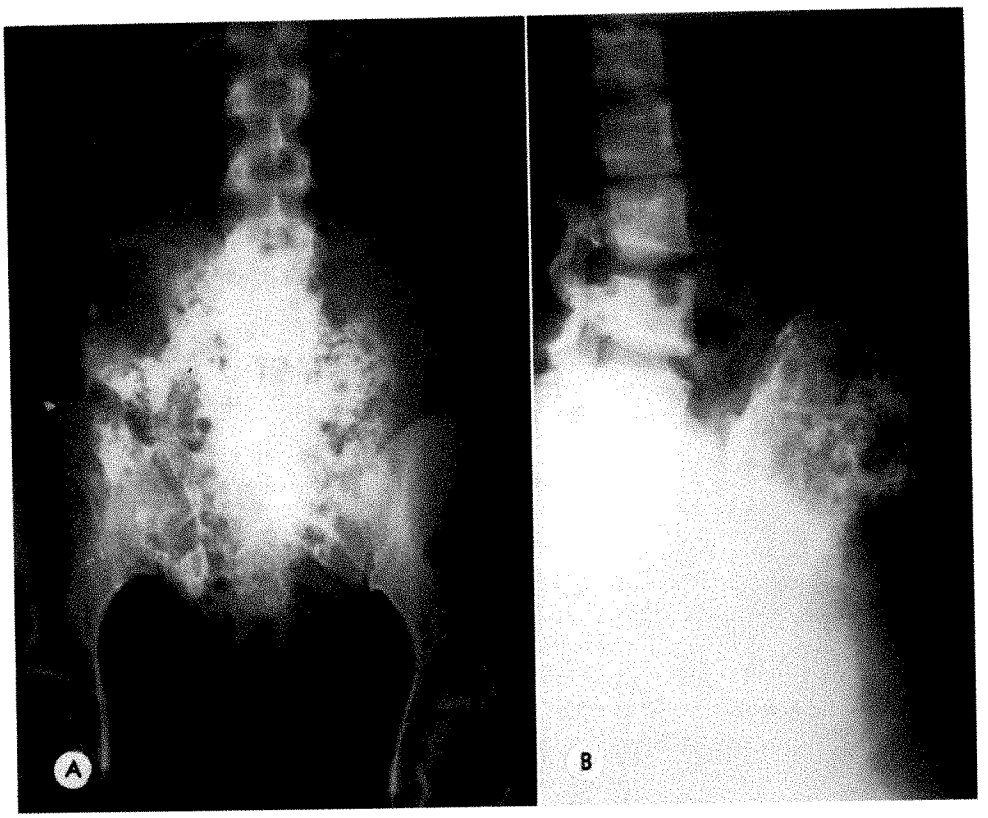


FIG. 2. Case II. (*A*) Anteroposterior and (*B*) lateral hysterograms show the multiple filling defects producing the so-called "honeycomb" pattern of the hydatidiform mole. (Courtesy of Dr. James W. Ryel, St. Judes Hospital, Fullerton, California.)

fundus corresponded to 22 weeks of gestation. Her hemoglobin was noted to be 6.5 gm. per cent, HCG levels were elevated and urinary albumin was 4+. The plain roentgenogram of the abdomen revealed no fetal skeleton. Hysterography was then performed and showed the typical "moth-eaten" appearance of a hydatidiform mole (Fig. 2, *A* and *B*).

Comment. In this woman, the hydatidiform mole was complicated by pre-eclampsia, anemia, and severe hemorrhage that will occur with spontaneous evacuation.

DISCUSSION

Prompt and early diagnosis of hydatidiform mole will preclude the development of pre-eclamptic toxemia, anemia, and the hemorrhage associated with spontaneous unattended evacuation. Also, it is hoped that the incidence of the dreaded complication of choriocarcinoma might be lessened by the more early diagnosis of its precursor, hydatidiform mole. We feel that hysterography has a large role to play in detection of hydatidiform moles at approximately 12 to 14 weeks of gestation. At this time there is usually no history of passage of molar tissue, the uterus may or may not be inordinately enlarged, and often the HCG levels are equivocal. The fetal skeleton often does not visualize normally at this early date,[3] and therefore the clinician is faced with a diagnostic dilemma.

Even as late as 16 weeks of gestation, if the patient has not passed "grapes," a mole might be simulated by a multiple pregnancy since, in this latter instance, the fetal skeleton still might not be visible on roentgenographic study. Here, hysterography will quickly and effectively establish the diagnosis.

Apelo and Cunanan[1] described 42 cases of hysterography without complication, except for 1 case of mild infection. The pos-

sibility of washing trophoblastic material into the venous sinuses was considered, but close observation of these patients revealed no instance of choriocarcinoma. Of the 20 cases of hysterography done by a transabdominal approach, 19 were diagnostic, and there was only 1 instance of failure to demonstrate a mole roentgenographically. Torres and Pelegrina[18] reported 8 cases with a diagnosis established in 7. In the other, a normal fetus was recognized and carried to term, and a normal viable baby was delivered. Cheng[5] described 11 cases, of which the typical honeycomb appearance of hydatidiform mole was seen in 10. The remaining case turned out to be a normal pregnancy which subsequently went to term, and a healthy fetus was delivered. In his experience no complications were noted. MacClain[9] used amniography in 75 patients in a variety of obstetrical problems, including 1 case of hydatidiform mole diagnosed at 10 weeks of gestation. He claims no evidence of premature labor due to the procedure. No instance of trauma to either the fetus or the mother was noted in his series.

Another mode of detecting hydatidiform moles is pelvic arteriography which was first described by Borell and Fernström[2] in 1961. They noted 5 cases successfully diagnosed as early as 13 weeks; however, 3 out of the 5 cases were diagnosed at 15 weeks or later. Wilson *et al.*[20] discuss 4 cases in which comparison is made between amniography and pelvic arteriography. They conclude that either of the procedures will confirm the diagnosis. Wholey[19] states that patients at 12 to 14 weeks of gestation who present with abnormal vaginal bleeding are ideal candidates for angiography. He believes, however, that the angiographic differences between normal pregnancy and hydatidiform mole are frequently minimal at this early stage. In his experience, as well as of others, the finding of fewer and less well opacified intervillous spaces has been the most reliable finding.

Since, in the application of pelvic arteriography, serial filming and fluoroscopy are employed, one might wonder as to the radiation hazard to a live fetus at, for example, 12 weeks of gestation when the diagnosis of threatened abortion is established rather than that of hydatidiform mole. In 1952, Russell and Russell[14] reported that leukemia and malignancies developed twice as often in children born to women subjected to roentgen pelvimetry during pregnancy as in children not irradiated *in utero*. In 1962, MacMahon[10] reviewed the entire literature on the subject of the relationship of roentgen-ray exposure *in utero* and cancer in childhood and concluded, "It may be prudent to recognize that at the present time there is more in favor of the existence of such a relationship than there is against it." Hicks and D'Amati[8] have shown that single doses as low as 10 r have caused a widespread effect in the developing rat brain. Rugh[13] states that there is no question but that the penetrating ionizing radiations from 5 r upward can produce permanent, irrepairable effects on the rodent embryo. Because of the results of such animal experiments, radiologists in Denmark suggest a therapeutic abortion in any woman in whom the embryo received from 1 to 10 r. Depending on the type of equipment, length of fluoroscopic time in the placement of catheters, the number of sequential films exposed, it would seem possible to approximate these figures.

Faced with the problem of differentiating a mole from incomplete or threatened abortion at an early stage of pregnancy, would it not be more logical to subject the patient to a single anteroposterior roentgenographic exposure that is virtually diagnostic and without serious hazards than to proceed with arteriography?

SUMMARY

In the earlier periods of gestation, from approximately 12 to 14 weeks, the clinician is often faced with a diagnostic dilemma in the differential diagnosis of hydatidiform mole from incomplete or threatened abortion.

Often at this stage of gestation the

patient presents with vaginal bleeding but has not passed molar tissue and, on physical examination, the uterus may not be unduly enlarged.

High urinary gonadotropin levels at this stage of gestation may be seen in normal pregnancy.

The absence of roentgenographic visualization of a normal fetal skeleton is again within the range of normal at this early stage.

We feel that the best approach in making this differential diagnosis is by use of transabdominal hysterography. This method is virtually diagnostic and without serious hazard.

Edward I. Greenbaum, M.D.
2101 Ponderosa Street, Apt. 5C
Santa Ana, California 92701

I wish to thank Mr. Goodwin O'Neal for his excellent reproductions; thanks also to Mrs. Dona Jones and Mrs. Gayle Keyes for their assistance.

REFERENCES

1. Apelo, R., and Cunanan, R. Value of hysterogram in diagnosis of hydatidiform mole: report of 42 cases. *Philippine J. Surg.*, 1966, *21*, 283–287.
2. Bayan, F., and Apelo, R. Direct and positive diagnosis of hydatidiform mole. *Philippine J. Surg.*, 1957, *12*, 1–6.
3. Borell, U., and Fernström, I. Hydatidiform mole diagnosed by pelvic angiography. *Acta radiol.*, 1961, *56*, 113–118.
4. Bourne, W. A Synopsis of Obstetrics and Gynecology. John Wright & Sons, Ltd., Bristol, 1957, pp. 10–11.
5. Cheng, W-C. Value of amniography in early diagnosis of hydatidiform mole. *J. Obst. & Gynaec. Brit. Emp.*, 1967, *74*, 753–756.
6. Douglas, G. W. Diagnosis and management of hydatidiform mole. *Surg. Clin. North America*, 1957, *37*, 379–392.
7. Goldstein, P., and Reid, D. E. Recent developments in management of molar pregnancy. *Clin. Obst. & Gynec.*, 1967, *10*, 313–317.
8. Hicks, S. P., and D'Amati, C. J. Low dose radiation of developing brain. *Science*, 1963, *141*, 903–905.
9. MacLain, C. R., Jr. Amniography: versatile diagnostic procedure in obstetrics. *Obst. & Gynec.*, 1964, *23*, 45–50.
10. MacMahon, B. Prenatal x-ray exposure and childhood cancer. *J. Nat. Cancer Inst.*, 1962, *28*, 1173–1191.
11. Massee, J. S. Hysterography: new aid in diagnosis of hydatidiform mole. *Minnesota Med.*, 1967, *50*, 751–752.
12. Robbins, S. L. Textbook of Pathology. W. B. Saunders Company, Philadelphia, 1957, 1059–1063.
13. Rugh, R. Impact of ionizing radiations to embryo and fetus. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1963, *89*, 182–190.
14. Russell, L. B., and Russell, W. L. Radiation hazards to embryo and fetus. *Radiology*, 1952, *58*, 369–377.
15. Savignac, E. M. Roentgen amniography: valuable and safe aid to obstetrical diagnosis. *Radiology*, 1963, *60*, 545–558.
16. Schreibner, M. H., and Morettin, L. B. Antepartum prediction of fetal maturity. *Radiol. Clin. North America*, 1967, *5*, 21–28.
17. Taymor, M. L. Bioassay and immunoassay of human chorionic gonadotropin. *Clin. Obst. & Gynec.*, 1967, *10*, 303–312.
18. Torres, A. H., and Pelegrina, I. A. Transabdominal intrauterine contrast medium injection. *Am. J. Obst. & Gynec.*, 1966, *94*, 963–968.
19. Wholey, M. H. Evaluation of arteriography in obstetrics. *Radiol. Clin. North America*, 1967, *5*, 121–131.
20. Wilson, G., Colodny, S., and Weidner, W. Comparison of amniography and pelvic angiography in diagnosis of hydatidiform mole. *Radiology*, 1966, *87*, 1076–1079.

A ROENTGENOLOGIC RULE AND PELVIMETRY TECHNIQUE*

By T. H. JOHNSON, JR., M.D.,† *and* T. A. REAGAN, R.T.
MEMPHIS, TENNESSEE

ROENTGENOLOGIC mensuration in pelvimetry as well as other areas of radiology is often complicated by human error or less than optimal roentgenographic equipment. Accurate measurements may be obtained by mathematical equations for the magnification factor or physical placement of a measuring apparatus in the roentgen field at the time of the exposure. These methods may lead to miscalculations or repeated filming. Another approach to mensuration seemed advisable to eliminate this repeated filming and maintain accuracy.

MATERIAL AND METHOD

A copper rule was prepared marked with 1 cm. and $\frac{1}{2}$ cm. reference points (Fig. 1). Using a 40 inch focus-film distance with a standard roentgenographic table, the copper plate was roentgenographed at successive 1 cm. distances from the tabletop over the usual range of patient thickness. The 2 inch space between film and tabletop of a standard table was considered and figured into the preparation. The spacing of a 4 way movable tabletop is not a standard 2 inches, and a slight deviation of accuracy is present when this table is used or when the cassette is placed on a table directly under the patient.

A composite rule was prepared from these roentgenograms to allow direct application to the film, knowing only the distance of the point or lesion from the tabletop. No mental calculation is therefore necessary.

The rule series can be kept at the interpretation desk for direct application to the roentgenograms. When applying to measurements other than pelvimetry, the rule scale is chosen corresponding to the centimeter distance of the lesion from the tabletop. The level is predetermined from a lateral roentgenogram or physical measurement information.



FIG. 1. A prepared copper centimeter rule was roentgenographed at 1 cm. distances from the tabletop with a 40 inch focus-film distance. From these roentgenograms a finished rule was fashioned.

DISCUSSION

A specific application for this radiology rule could be short distance pelvimetry (40 inch focus-film distance). In short distance pelvimetry, technologists sometimes forget to include the metallic rule or position the rule so that it is overpenetrated and difficult to visualize with a standard view box. Using this rule and knowledge of patient thickness at the pubis

* From the Department of Radiology, University of Tennessee, Memphis, Tennessee.
† Associate Professor. Present Address: Department of Radiology, University of Pittsburgh, Pittsburgh, Pennsylvania.

in the anteroposterior position and laterally at the greater trochanters, it is simple to place the rule scale at the proper level and obtain the readings directly from the roentgenogram. The anteroposterior pelvimetry view is roentgenographed as usual with a 40 inch focus-film distance. No extraneous apparatus is positioned at the time of roentgenography, thus eliminating one of the sources of error that occur. The pubic symphysis to the tabletop measurement is made as usual for an anteroposterior view as illustrated in Figure 2. The rule scale is then chosen as 10 cm. less than the anteroposterior measurement, which is the level of the birth canal at the ischial spine. The lateral pelvimetry roentgenogram is performed as usual with a 40 inch focus-film distance and the patient in the true lateral position as shown in Figure 3. The patient thickness is measured at the level of the trochanters, as is done routinely to establish optimal roentgenographic density.

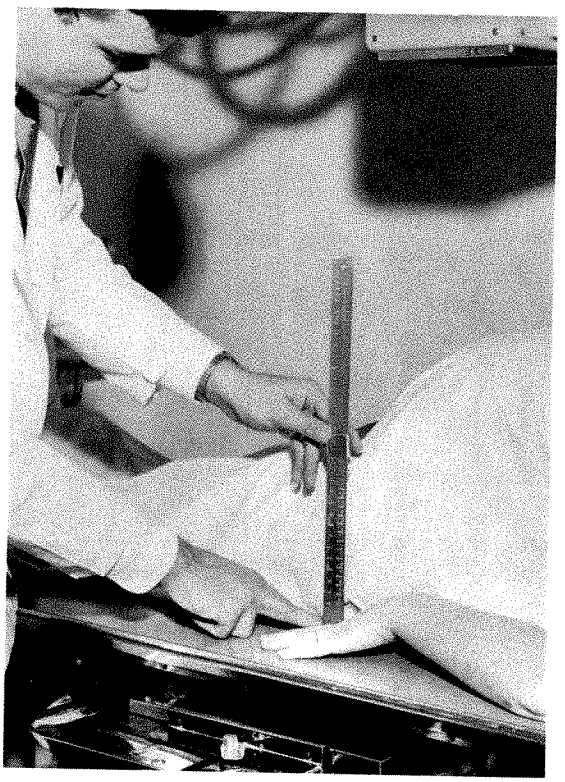


FIG. 2. The anteroposterior measurement is made from the symphysis pubis to the tabletop.



FIG. 3. The lateral measurement is made at the level of the greater trochanters.

The rule is chosen as one-half the measured thickness, which would be the midline of the bony pelvis (birth canal). These measurements can be recorded on the request-report form, so the exact interpretation can be made easily.

Pelvimetry measurements are made in the usual manner at inlet, midpelvis and outlet in their anteroposterior and lateral positions, thus establishing the measurements necessary for the inlet, midpelvis and outlet for accurate pelvimetry mensuration (Fig. 4).

The steps necessary for pelvimetry with this rule are as follows:

Anteroposterior View

1. Position as for any anteroposterior pelvic roentgenogram.
2. Use a 40 inch focus-film distance.
3. Measure the patient with standard roentgenologic calipers through the pubic symphysis. (These measuring points give the most accurate calculating points and

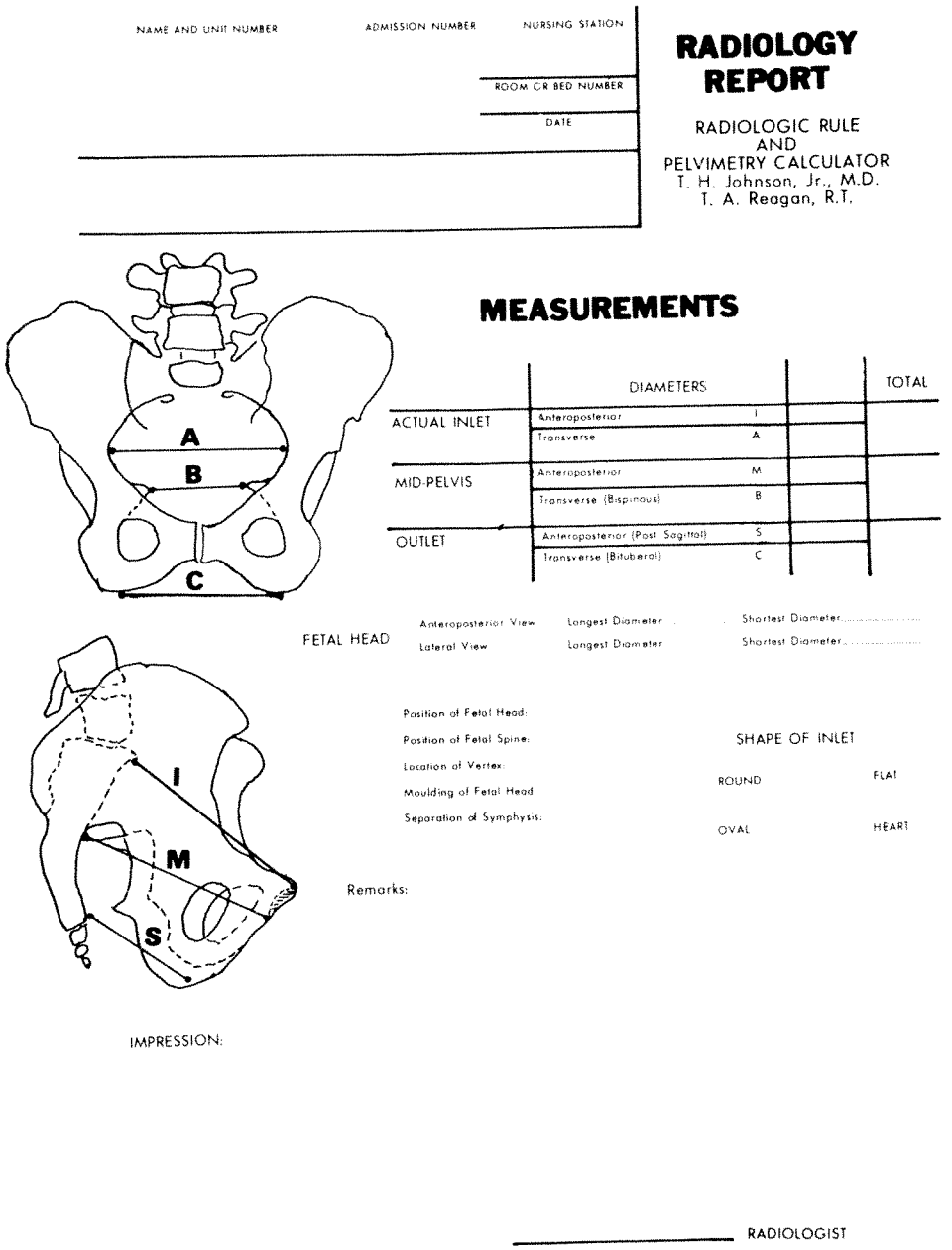


Fig. 4. This report form is used to indicate the results of measurements. The drawing verifies the sites and positions measured.

also provide maximal technical factors for the roentgenograms. It is mandatory to measure even if phototimed exposures are used.)

4. Center central ray 1½ inches above symphysis.
5. Record measurement on request form and roentgenograph if possible.
6. The centimeter scale to be used is 10 cm. less than the anteroposterior measurement.

Lateral View

1. Position as for any lateral pelvic roentgenogram. A perfect lateral is a must for accuracy.

2. Use a 40 inch focus-film distance.
3. Measure the patient with calipers through the greater trochanters. (These measuring points give the most accurate calculating points and also provide maximal technical factors for the roentgenogram. It is mandatory to measure even if phototimed exposures are used.)
4. Center central ray $1\frac{1}{2}$ inches above trochanters.
5. Record measurement as in the anteroposterior projection.
6. The centimeter scale to be used is one-half of the measurement.

If a 6 foot focus-film distance is used, the magnification factor is 0.96 of the apparent image. This corresponds to the 7 cm. scale of this magnification ruler and thus the 7 cm. scale may be used for direct reading from the roentgenogram.

SUMMARY

A roentgenologic rule has been developed for easy accuracy at the interpretation desk without mental calculations. The interpreter may apply the rule directly to the roentgenograms, choose the proper scale for the depth of the lesion and read off the real size of the pathology.

The rule lends itself well to pelvimetry and a technique is outlined.

Thomas H. Johnson, Jr., M.D.
Department of Radiology
University of Tennessee, Chandler Building
865 Jefferson Avenue
Memphis, Tennessee 38103

REFERENCES

1. CLARK, K. C. Female reproductive system, pelvimetry. In: Positioning In Radiology. Eighth edition. Intercontinental Medical Book Corporation, New York, 1964.
2. EASTMAN, N. J., and HELLMAN, L. M. Eastman's Obstetrics, William's Obstetrics. Thirteenth edition. Appleton-Century-Crofts, New York, 1966.
3. JOHNS, H. E. The Physics of Radiology. Second edition. Charles C Thomas, Publisher, Springfield, Ill., 1961.
4. MERRILL, V. Roentgen Pelvimetry: Atlas of Roentgenography. Third edition. C. V. Mosby Company, St. Louis, 1967, pp. 758–772.

RECOVERY OF DETACHED INTRAVASCULAR CATHETER OR GUIDE WIRE FRAGMENTS*

A PROPOSED METHOD

By JOSEPH L. CURRY, M.D.
EASTON, PENNSYLVANIA

RECOVERY of a broken catheter or guide wire fragment from the aorta, vena cava, or other large vessel may require a formidable surgical procedure such as thoracotomy, laparotomy, or pelvic surgery with extraperitoneal approach to the iliac arteries. With the Seldinger technique of catheter arteriography, careful observance of well-established principles minimizes the dangers of intravascular detachment of a catheter or guide wire fragment. Nevertheless, the potential hazard of such accidents does exist,[1,2,3] even with meticulous quality control by the manufacturers of arterial catheter materials and guide wires.

This communication was occasioned by the severance of a polyethylene catheter in the aorta. The catheter† had been passed by the Seldinger method into the aortic arch through a left axillary artery insertion. The catheter tip was then guided down the aorta and entered the superior mesenteric artery. Moderate rotation and retraction with guide wire in place caused the catheter to "shear in two" at the level of the aortic arch. Severance of the catheter became ob-

† Polyethylene, white, B-D×.035, fabricated 3 weeks prior to use, stored in original purchase package for 9 months in a dry lightproof box, and immersed in 1:1,000 detergicide solution 6 hours prior to use.

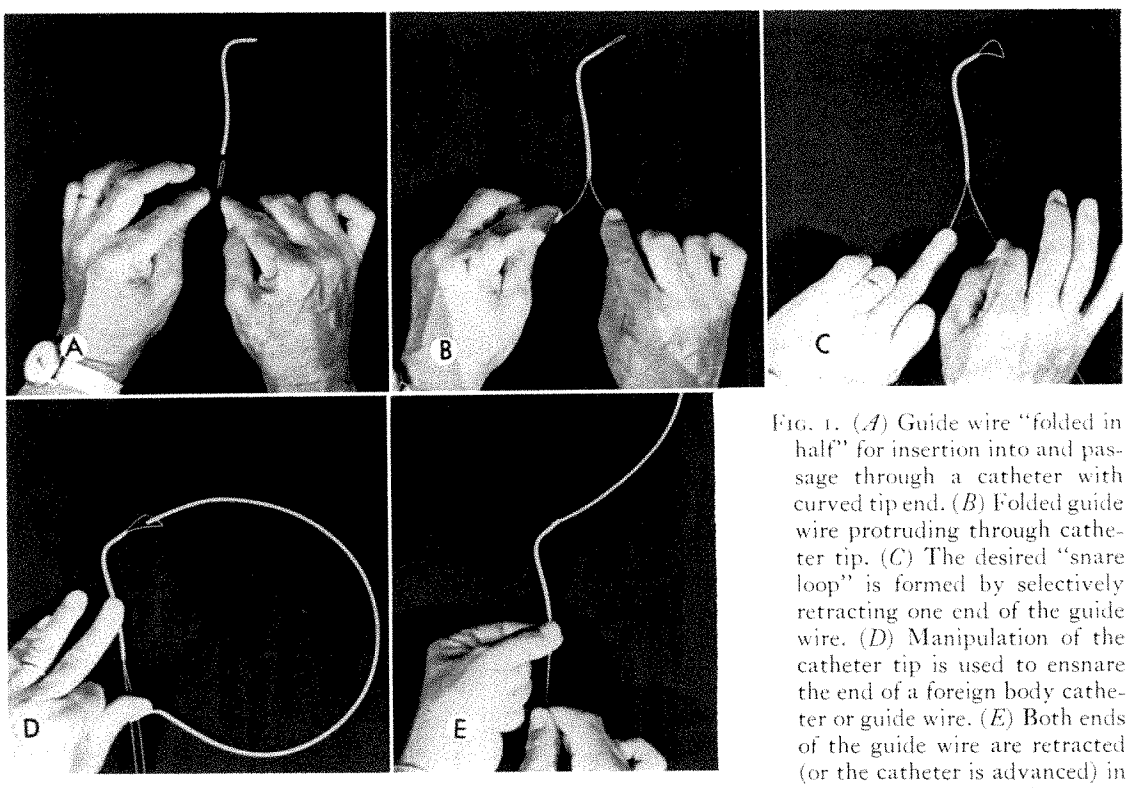


FIG. 1. (*A*) Guide wire "folded in half" for insertion into and passage through a catheter with curved tip end. (*B*) Folded guide wire protruding through catheter tip. (*C*) The desired "snare loop" is formed by selectively retracting one end of the guide wire. (*D*) Manipulation of the catheter tip is used to ensnare the end of a foreign body catheter or guide wire. (*E*) Both ends of the guide wire are retracted (or the catheter is advanced) in order to close the loop. This immobilizes the foreign body against the catheter tip for withdrawal.

* From the Department of Radiology, the Easton Hospital, Easton, Pennsylvania.

vious when the catheter was retracted from the axilla. At this point, the guide wire was seen to retract with the axillary catheter segment, leaving behind the detached catheter segment in the aorta. The result was a detached catheter fragment with one end in the superior mesenteric artery and the other in the aortic arch. Although other complications have occurred, this was the first incident of this type in a series of over 3,000 catheter angiographies.

Efforts were made to ensnare the end of the detached catheter with a guide wire passed through a second intra-aortic catheter in the hope of retracting the catheter tip into a peripheral artery location for simple removal by arteriotomy. These efforts were unsuccessful, and the catheter was removed at laparotomy by superior mesenteric arteriotomy.

This distressing experience promoted the concept of an efficient, nonoperative removal of broken catheter or guide wire foreign bodies from the aorta or other large vessels. The method suggested involves the use of a special guide wire made into a snare which can be passed through the tip of a curved catheter with ease (Fig. 1, *A-E*).

The technique involves 4 basic steps:

(1) A teflon (7F or 8F) catheter with a reversed-curve tip is inserted into a peripheral artery or vein by the Seldinger method, and its end is guided to a position near the tip of the detached catheter or guide wire.

(2) A 0.021 or 0.028 inch diameter guide wire (coiled exterior with fixed core) is tightly "folded" into a crease at its midportion (Fig. 1*A*). This allows the operator to pass the creased end of the guide wire through the teflon ‡ catheter tip (Fig. 1*B*).

(3) One end of the guide wire is slowly withdrawn from the catheter, while the other end is immobilized. This allows selective formation of a desired loop under fluoroscopic guidance (Fig. 1*C*). Manipulation of the curved catheter tip is used to ensnare the end of the foreign body catheter or guide wire (Fig. 1*D*).

(4) Finally, both ends of the guide wire are retracted together, so that the closed loop snares the foreign body snugly against the tip of the catheter for withdrawal (Fig. 1*E*). In this respect, the instrument performs similarly to a noncutting tonsil snare. An alternate method of closing the loop is to advance the catheter on the folded guide wire.

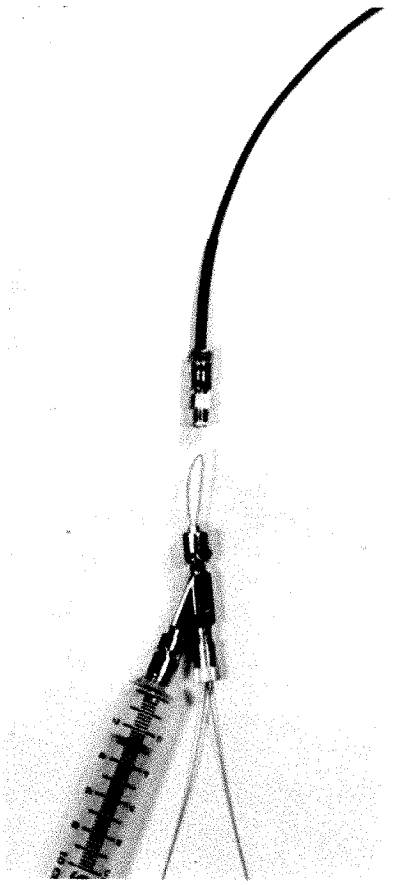


Fig. 2. Modified side-arm catheter irrigator as a proposed broken catheter and guide wire retriever.§ This provides a closed system which may be irrigated while the folded guide wire snare is in place.

‡ Teflon seems desirable for passage of a folded guide wire because of its smooth, low-friction surface.

§ Available from Cook Incorporated, Bloomington, Indiana.

An *in vitro* trial of this method strongly suggested the need for a coiled guide wire over a fixed core, the type commonly used in catheter arteriography. This provides a sufficient coefficient of friction to firmly fix the foreign body against the catheter tip during withdrawal (Fig. 1*E*).

In order to provide a closed system which also allows irrigation of the catheter with the guide wire loop in place, a specially constructed side-arm catheter irrigator has been devised (Fig. 2). The 2 open ends of the folded guide wire are exteriorized through a neoprene gasket which allows retraction and advancement of the guide wire. No leakage occurs when the gasket is tight, and the side-arm allows irrigation of the closed system.

SUMMARY

1. A method is proposed for nonoperative removal of detached guide wire or catheter fragments from the aorta or other large vessels.

2. Further investigation of this technique would seem justified as a potential solution to a rare but formidable complication of catheter angiography.

Department of Radiology
Easton Hospital
21st and Lehigh Streets
Easton, Pennsylvania 18042

Appreciation is expressed to Arthur Burd, R.T. and Anthony Getz, R.T. of the Radiology Department, Easton Hospital, Easton, Pennsylvania, for technical assistance and photography.

REFERENCES

1. Coblentz, D. R. Radiographic detection of plastic catheter embolus. *Col. Med.*, 1966, *105*, 357–360.
2. Cope, C. Intravascular breakage of Seldinger guide wires. *J.A.M.A.*, 1963, *12*, 139–141.
3. Lang, E. K. Prevention and treatment of complications following arteriography. *Radiology*, 1967, *88*, 950–956.

VOL. 105, NO. 4

SKIN EXPOSURE FROM HANDLING SYRINGES CONTAINING RADIOACTIVE ISOTOPES*

By R. S. CLAYTON, M.D., J. E. WHITE, M.D., M. BRIEDEN *and* A. RODRIGUEZ, R.T.
EL PASO, TEXAS

A TREMENDOUS increase in the use of injectable diagnostic radioisotopes occurred following the development of organ scanning techniques. The dosage of the commonly used radioisotopes was in the microcurie range (50–600) until the advent of generators which made feasible the use of the short half-life isotope, technetium 99m. Now, with the increased utilization of brain-scanning using from 5 to 20 mc of Tc^{99m}, radiation exposure to the skin of the fingers of personnel holding syringes becomes potentially significant.

Usually the same technician each day loads syringes with the radioisotope to be injected. In each loading operation, the syringe is held by the same fingers. Thus, *the same skin of the same fingers* is repeatedly in contact with the syringe. If the same technician performs the intravenous injection, again the same areas of skin are exposed. If another technician, a nurse, or a physician injects the material, it is usually the same person each day, and again, *the same skin of the same fingers* is exposed, day after day, year after year.

Inquiry of the appropriate licensing authorities[1,2] and a search of the literature yielded no reports of measurement of skin exposure under the above described circumstances.

Whether the cumulative exposure to the skin is or is not significant, the amount of radiation exposure should be known. If insignificant exposure results from handling a normal volume of these procedures, at least all parties concerned will be reassured.

On the other hand, if potentially injurious amounts of radiation could be accumulated over a number of years, steps to minimize the exposure should be taken. Aside from actual skin damage, the subject has medicolegal implications. Simple measures are available which can reduce exposure to very low levels.

Thermoluminescent dosimeters (TLD) of reasonable accuracy and small size have become commercially available the past 2 or 3 years. Until the development of these dosimeters, there was no feasible method to measure accurately the exposure to skin in contact with syringes containing radioactive materials.

EXPERIMENTAL METHOD

Plastic syringes were loaded with the usual diagnostic amounts of Au^{198} and I^{131} in 1 ml. tuberculin syringes, Hg^{203} in 2.5 ml. syringes, and Tc^{99m} in 10 ml. syringes. A thermoluminescent dosimeter* was taped to an index finger at the point normally in contact with a syringe, a plastic disposable glove was drawn on, and the dosimeter was held against the syringe for 60 seconds (Fig. 1). Three observations were made at each point and the readings averaged.

Observations were also made against the unloaded portion of the syringe. This observation was made near the rear of the barrel of the syringe (Fig. 2).

Blenderm surgical tape was used to hold the dosimeter to the finger. The readings might have been higher without interposition of the tape.

The amounts of radioisotopes used and the averaged readings are tabulated in Table 1.

Also shown in Table 1 are rough estimates of the number of exposures required to accumulate 100 r to the skin.

* R. S. Landauer Co., Matteson, Illinois.

* From the Department of Radiology, the Hotel Dieu Hospital, El Paso, Texas.

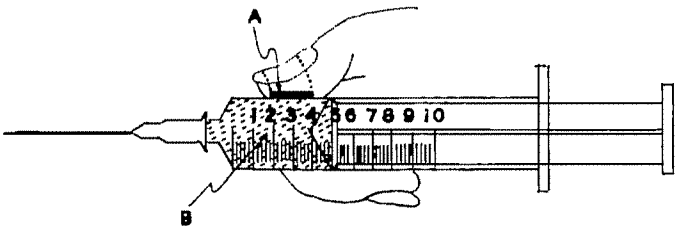


FIG. 1. The dosimeter was held against the syringe for 60 seconds. (*A*) L:F thermoluminescent dosimeter (TLD). (*B*) Radioactive solution.

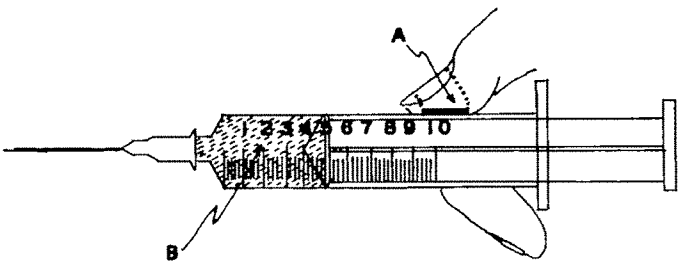


FIG. 2. Observation made against the unloaded portion of the syringe, near the rear of the barrel. (*A*) L:F TLD. (*B*) Radioactive solution.

DISCUSSION

Various factors can influence the dose rate at the surface of the syringe. Principal among these factors are: (1) the volume of liquid required to contain the desired amount of radioactivity; the larger the volume, the lower the dose rate at any given point; (2) the composition, wall thickness, and diameter of the syringe; (3) the amount of radioactivity being used; (4) the specific radioactive element involved.

It is apparent from the readings over the loaded and unloaded areas of the syringe that 2 important factors influence exposure to the skin: (1) the portion of syringe held during loading or injecting; and (2) the time the syringe is held.

TECHNIQUE TO MINIMIZE EXPOSURE

To minimize exposure of the skin, the syringe should be held by the portion of the barrel farthest from the radioactivity, and for the shortest time possible.

In loading a syringe, one should hold the barrel by the extreme rear-end, quickly aspirate the necessary volume, and lay the syringe down promptly.

For intravenous injection, every detail for venipuncture should be prepared before the syringe is picked up. If available

TABLE I

AMOUNTS OF RADIOISOTOPES USED AND AVERAGED READINGS

Radioactive isotope	Activity	Volume	Loaded portion of syringe, 60 second contact	Injections per 100 roentgens	Unloaded portion of syringe, 60 second contact	Injections per 100 roentgens
Tc^{99m}	10.9 mc	1 cc.	160 mr	600	8 mr	12,100
Tc^{99m}	5.6 mc	1 cc.	83 mr	1,200	9 mr	11,000
Au^{198}	100 μc	0.28 cc.	12 mr	8,330	8 mr	12,100
Hg^{203}	100 μc	0.59 cc.	26 mr	3,800	12 mr	8,000
I^{131}	200 μc	0.3 cc.	40 mr	2,500	5 mr	20,000

veins are not large, and the venipuncture promises to be difficult, start an intravenous infusion of normal saline and make sure the solution is entering the vein lumen and that no leakage into the tissues is occurring. Then, using a 22 gauge or smaller needle, insert the needle for injection of the radioactive solution into the infusion tubing close to the needle in the vein. Next, close the clamp on the infusion tubing, inject the radioactive solution, then release the infusion clamp to flush all the activity into the vein. While the flushing is occurring, the injection syringe can be rinsed of all activity and the needle removed from the infusion tubing. Finally, the infusion needle is removed from the patient. In either case, whether injection is made directly into a a vein, or into tubing, always hold the syringe by the extreme rear of the barrel.

SUMMARY

Exposure to the skin of fingers holding syringes containing diagnostic dosages of radioactive isotopes has been measured for one set of circumstances. Obviously, exposure under other circumstances may be higher or lower.

Simple measures to minimize exposure are described.

All personnel handling radioisotopes under similar circumstances should be encouraged to practice techniques which will minimize exposure to the skin as well as to the entire body.

R. S. Clayton, M.D.
Department of Radiology
Hotel Dieu Sisters' Hospital
1014 N. Stranton
El Paso, Texas 79902

REFERENCES

1. Division of Radiation Control, Texas State Department of Public Health, Austin, Texas. Personal communication.
2. Sagan, L. A. United States Atomic Energy Commission, Washington, D. C. Personal communication.

THE INDEPENDENT RADIATION MONITOR (I.R.M.)

By PAUL M. KROENING, M.D.,* *and* RAYMOND MUCHA†
TEMPLE, TEXAS

THE value of a device to indicate that a radiotherapy unit is emitting radiation can be appreciated by radiation therapists, physicists, and technicians. "Is the beam on?" becomes an urgent question at some time in every Radiation Therapy Department. A definitive "Yes" or "No" answer can be based upon a signal from an Independent Radiation Monitor (I.R.M.).

At the Scott and White Clinic, the need for an I.R.M. caused us to design and construct a simple, inexpensive ionization chamber which illuminates a light bulb when a given level of radiation is reached. The device is powered by batteries, and its performance is not affected by fluctuations in the house current. Designed as a safety device and not as an instrument to measure quality or quantity of radiation, the monitor is placed in a therapy room so that the technician observing the patient can see the indicator light through the viewing window. When the bulb glows, the observer knows that the shutters of the therapy unit are open and radiation is being emitted (Fig. 1).



Fig. 1. Independent radiation monitor (I.R.M.) in action. Technician observes both patient and monitor light.

Five independent radiation monitors are used in our Radiation Therapy Department. Four are placed in treatment rooms, and one serves the radium storage area where an indicator light over the doorway warns us if the safe is open. Each I.R.M. is adjusted to detect the lowest required level of radiation. For example, the I.R.M. setting in the superficial therapy room is low because the tiny cone emits such small amounts of radiation. Also the minimal setting must be above the level of radiation leakage from the head of the therapy unit. To assure reliable function, each monitor's batteries are changed routinely. The 1.5 volt batteries are changed monthly; the 9 volt battery is changed every other month. The sensitivity of the monitor is checked weekly.

To make an I.R.M. more attractive, it can be painted the same color as the therapy unit which it serves. Incidentally, the cost of the materials for an I.R.M. is less than $20.00 (Table 1).

TECHNICAL DESCRIPTION

In the I.R.M., current is produced by ionization in a detector chamber; and it operates a relay that controls an indicator light. The detector chamber (a can for tennis balls will suffice) contains a 5886 electron tube and a piece of copper tubing (0.25

* Chief, Radiation Therapy Department, Scott and White Clinic, Temple, Texas.
† Electronic Instrument Technician, Scott and White Memorial Hospital and Scott, Sherwood and Brindley Foundation, Temple, Texas.

TABLE I

MATERIALS FOR INDEPENDENT RADIATION MONITOR

Material	Quantity	Description	Cost*
Resistors (8)			$0.48
1/2 W, 10 per cent	1	15 ohm	
	1	820 ohm	
	1	2.2 k. ohm	
	1	4.7 k. ohm	
	1	27 k. ohm	
	1	47 k. ohm	
1/2 W, 5 per cent	1	100 k. ohm	
	1	180 k. ohm	
Transistors (4)	3	2N1605	2.58
	1	2N 404	
Batteries (3)	1	Eveready, No. 266 (9 volt)	1.36
	2	D cells (1.5 volt)	0.25
Relay	1	Potter-Brumfield, #RS5D 2.5 K	3.00
Box	1	Bud Cu3005A (3×4×5 inches)	1.25
Potentiometer	1	10 K	1.75
Electron tube	1	No. 5886 (Ratheon or Westinghouse)	5.00
Light bulb	1	General Electric, No. 49	0.17
Battery holder	1	Keystone, No. 176	0.38

* Prices quoted from Allied Industrial Electronics Catalog, No. 690, 1969. Allied Radio Corporation, Chicago, Illinois.

inches in diameter; 6 inches in length) for its central electrode. If the inside of the chamber is coated with varnish, the surface must be painted with a conductive agent.* The electronic tube and central electrode are mounted on a plastic disk which insulates them from the base of the chamber (Fig. 2, *A* and *B*). The relay should be modified mechanically to increase its sensitivity. This modification is accomplished by bending the clapper spring to lessen resistance to the magnetic flux and then decreasing the clapper-pole distance by bending the normally open contact downward.

* AQUA-DAG, GC Electronics Company, Los Angeles, California 90018.

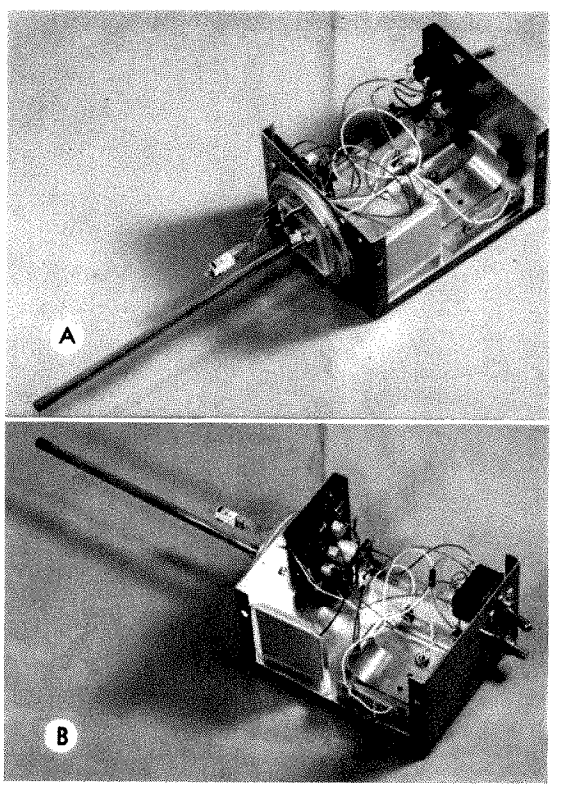


FIG. 2. Oblique views of independent radiation monitor with its ion chamber and sides removed. (*A*) Note mounting of the central electrode. (*B*) Note sensitivity adjustment (lower) knob and (upper) toggle knob, optional on-off switch.

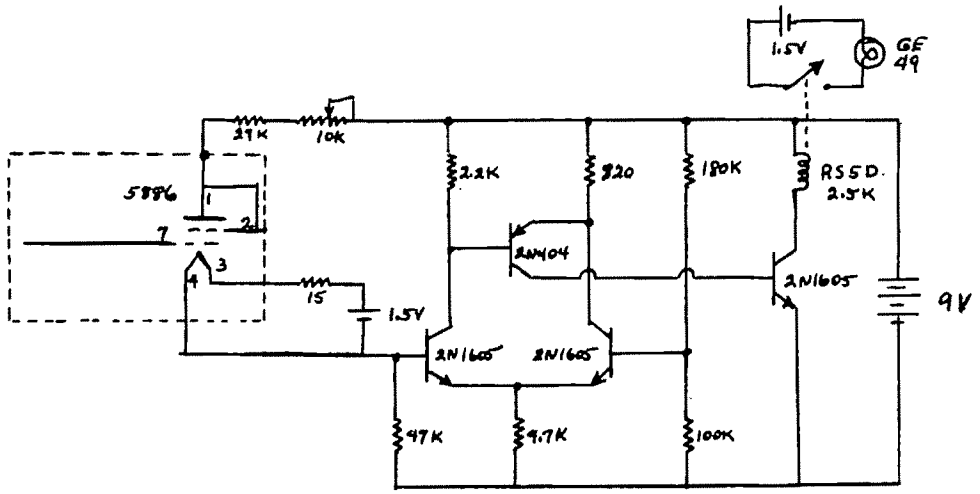


FIG. 3. Diagram of the independent radiation monitor circuit.

The normally closed contact is bent downward to just allow the normally open contact to open when the relay releases. A 10 K potentiometer is located on one end of the I.R.M. to facilitate adjustment of its sensitivity. An on-off switch is optional; not included on the circuit diagram (Fig. 3). Finally, the 1.5 volt batteries could be installed in parallel circuitry for longer yield.

SUMMARY

An independent radiation monitor (I.R.M.) is a reliable safety device for any radiation therapy room. It shows conclusively that the beam is "on." The I.R.M. is inexpensive and simple to construct.

Paul M. Kroening, M.D.
Department of Radiation Therapy
Scott and White Clinic
Temple, Texas 76501

The authors would like to thank Miss Karen Brothers for her help in constructing Scott and White's independent radiation monitors.

VOL. 105, NO. 4

THREE DIMENSIONAL ROENTGENOGRAPHY*

By J. B. GARRISON, D. G. GRANT, W. H. GUIER, *and* R. J. JOHNS
SILVER SPRING, MARYLAND

INFORMATION concerning the internal structure of an object may be obtained through the use of various roentgen-ray techniques. The advantage of the method described in this report over the related methods of laminagraphy, tomography and stereoroentgenography is that it allows the user to obtain a view of any plane in a three-dimensional object from a limited number of roentgenograms. Furthermore, the total radiation dosage required to observe a given volume is substantially reduced compared to these other methods.

GEOMETRY

Figure 1 shows the geometry used for taking a set of N roentgenograms.

- X_n are point sources of roentgen rays
- F_n are the roentgenographic films, with the plane of F_n parallel to the plane of F_m
- O is the object being roentgenographed
- P is a fixed point
- Q_nPX_n is a straight line with Q_nP and PX_n of constant length.

In addition, we have, for convenience, restricted the positions of X_n to lie in a plane parallel to the plane of the film. The restrictions on the geometry (X_nP and PQ_n of constant length and F_n parallel to F_m) permitted use of the Polytome at the Johns Hopkins Hospital for taking the tomograms, while the restriction that the X_n's lie in a plane parallel to the plane of the F_n's simplified the construction of the initial optical equipment. Using the Polytome we took 20 separate tomograms with the X_n being equally spaced along the circumference of a circle.

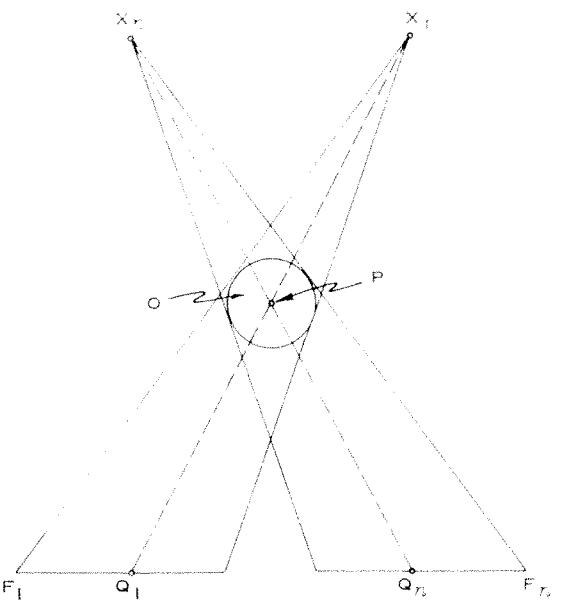


FIG. 1. Recording geometry.

Two different techniques have been devised for combining the N roentgenograms in the desired way. The principles underlying the first of these are shown in Figure 2.

- L_n are point light sources placed at the positions originally occupied by the X_n
- F_n^* are photoreduced copies of the F_n with the reduction equal to $|L_nQ_n^*|/|L_nQ_n|$ with $L_nQ_n^*PQ_n$ being a straight line, and the plane of the F_n^* being parallel to the plane of the F_n
- S is a moveable viewing screen.

We first note that, if the point light sources are turned on, the shadows cast by the F_n^* will exactly duplicate, in the plane of the F_n, the roentgenograms taken as indicated in Figure 1 (neglecting diffraction).

* From The Johns Hopkins University, Applied Physics Laboratory, Silver Spring, Maryland.
This work has been supported in part by the Department of the Navy, Contract number NOw-62-0604-c, Public Health Service Grant No. 5-S01-FR5378-06 and the Commonwealth Fund.

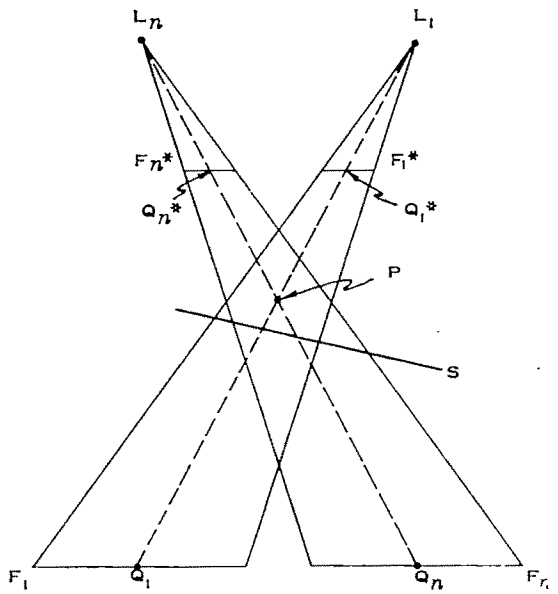


Fig. 2. Playback geometry.

It therefore follows that the image formed on screen S will be the reconstructed roentgenogram of a thin section defined by the intersection of the screen and the original object O.

A device based upon the principles depicted in Figure 2 has been successfully demonstrated and is shown schematically in Figure 3. A single 100 watt zirconium arc point source is used in conjunction with a mirror assembly to produce 20 virtual point sources. The reduced roentgen-ray negatives are mounted on a support ring which in turn is attached to the mirror assembly. Proper alignment of each negative is obtained by matching reference lines on the support ring with reference lines printed on each negative. Planar roentgen-ray images of the original object (*e.g.*, chimpanzee's skull) were observed by moving a viewing screen through the volume where the projected images superimpose. This system, which demonstrated the feasibility of the approach, was of course limited in resolution due to diffraction between the reduced negatives and the viewing screen.

An alternate technique which eliminates the image degradation due to diffraction has been demonstrated. This approach is shown schematically in Figure 4, *a* and *b*. The roentgen-ray negatives are photographically reduced to the size corresponding to location in the tomographic plane (the plane normally in focus for continuous motion). By means of a mirror assembly and wide angle lens the entire set

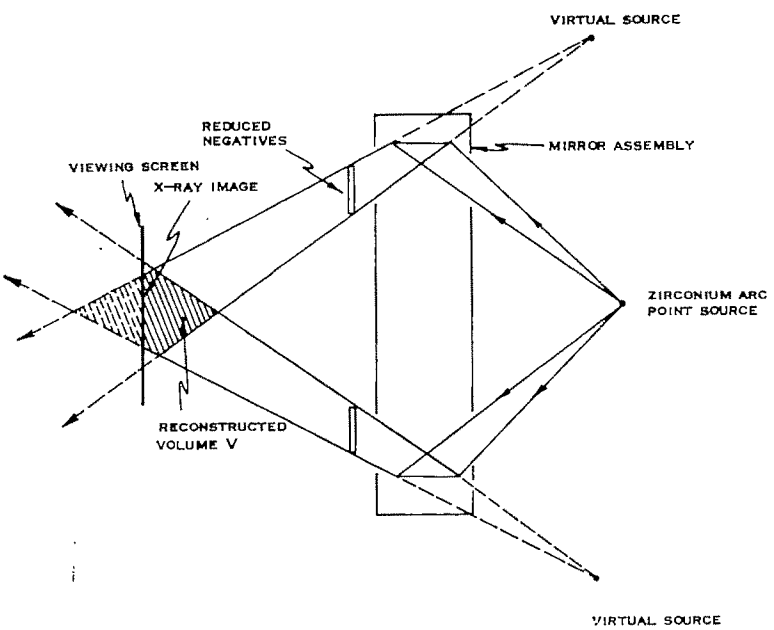


Fig. 3. Projector geometry.

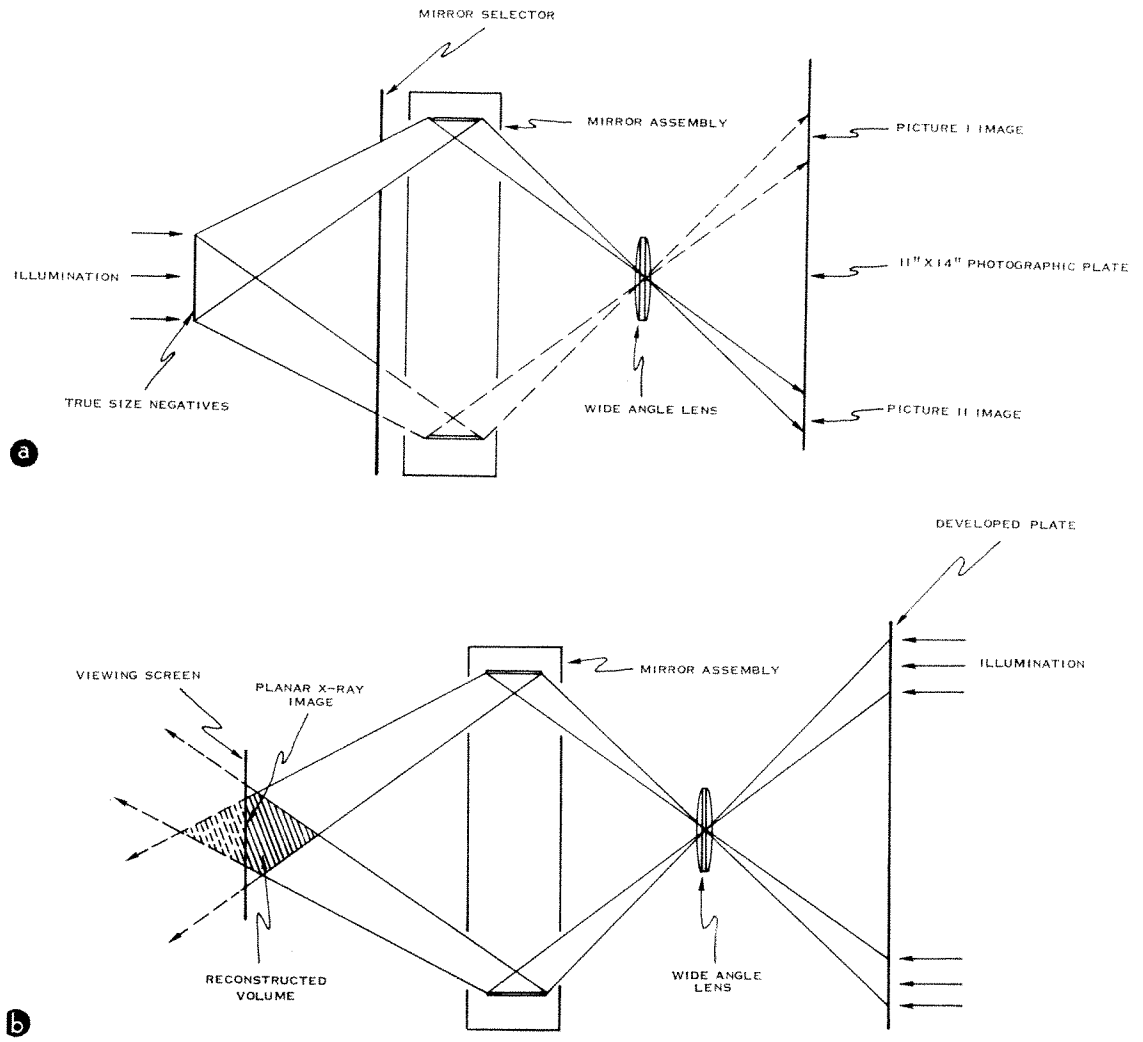


FIG. 4. (*a*) Three dimensional imaging-recording. (*b*) Three dimensional imaging-playback.

of 20 images are recorded separately on a single 11×14 inch photographic plate. The mirror selector is used to mask out all mirrors except the one corresponding to the negative being recorded. After recording, the photographic plate is developed and placed back into position. The plate is then illuminated from the back and the resulting 20 images are combined in space (Fig. 4*b*). Here again viewing of planar images is accomplished by a movable viewing screen.

Figures 5 through 8 show the optical system and typical results obtained to date using a chimpanzee skull. Figure 5 depicts the 11×14 inch camera back, wide angle lens, mirror assembly and viewing screen. Figure 6, *a* and *b* depicts 2 views of the chimpanzee's skull used for a subject. Figure 7 shows a sequence of images obtained by moving the viewing screen through the reconstructed chimpanzee skull in about 6 mm. increments. (These roentgenograms are reduced somewhat. The image on the viewing screen is the same size as the object.) The orientation of the screen was initially set approximately parallel to the base of the skull (*i.e.*, the plane shown in 6*b*) and remained fixed while the screen was translated through the reconstructed volume. A thin vertical wire was placed through the large hole in the base of the skull when the original set of

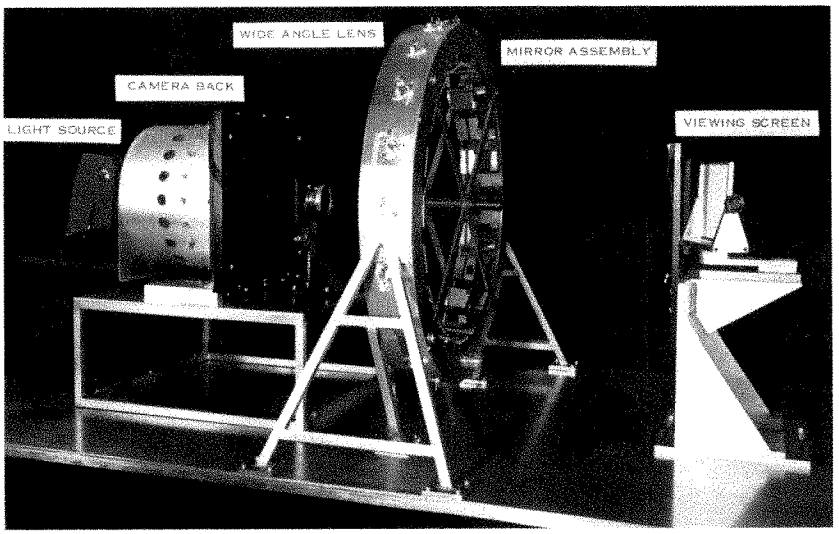


FIG. 5. Three dimensional imaging system.

20 roentgenograms was taken. This wire appears in cross section as a dot in the lower part of each roentgenogram. By rotating the viewing screen 90° about a vertical axis the wire can also be made to appear as a line. In addition, a small lead shot was placed near the eye of the skull and is clearly visible in Figure 7*i*. In Figure 8 the viewing screen was moved so as to image tilted planes. Figure 8, *a* and *b* shows planes rotated about a vertical axis while *c* and *d* show planes rotated about a horizontal axis: *d* is approximately parallel to the face of the skull.

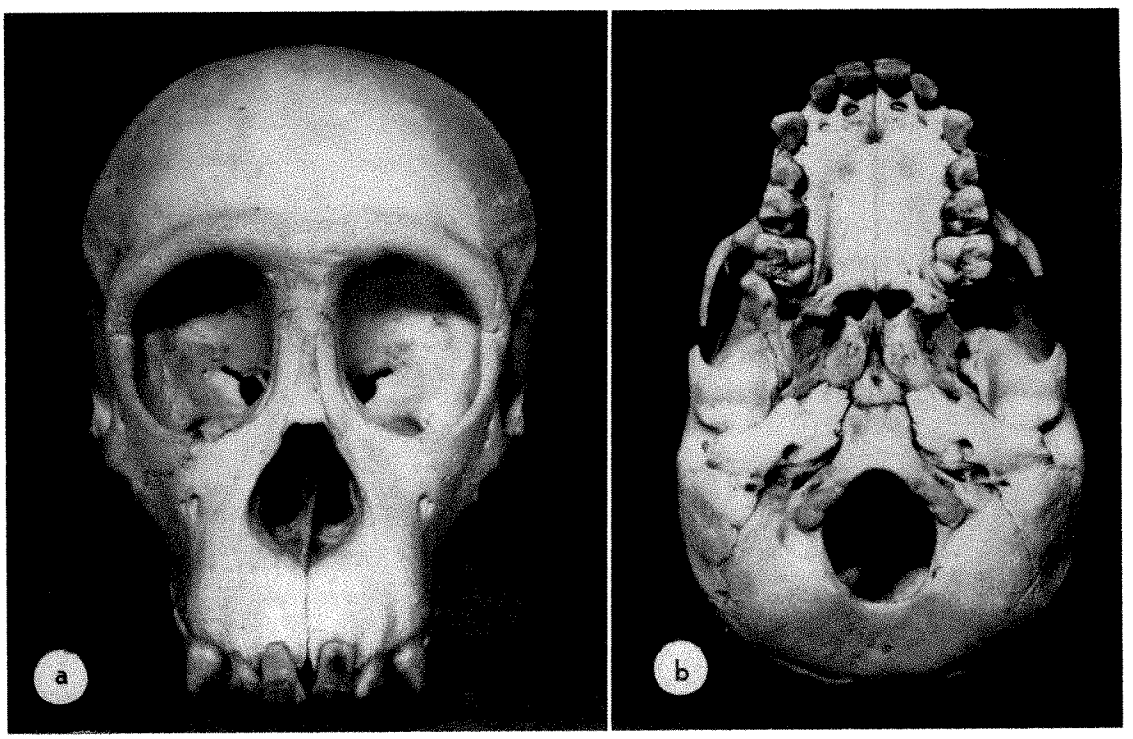


FIG. 6. (*a* and *b*) Chimpanzee skull.

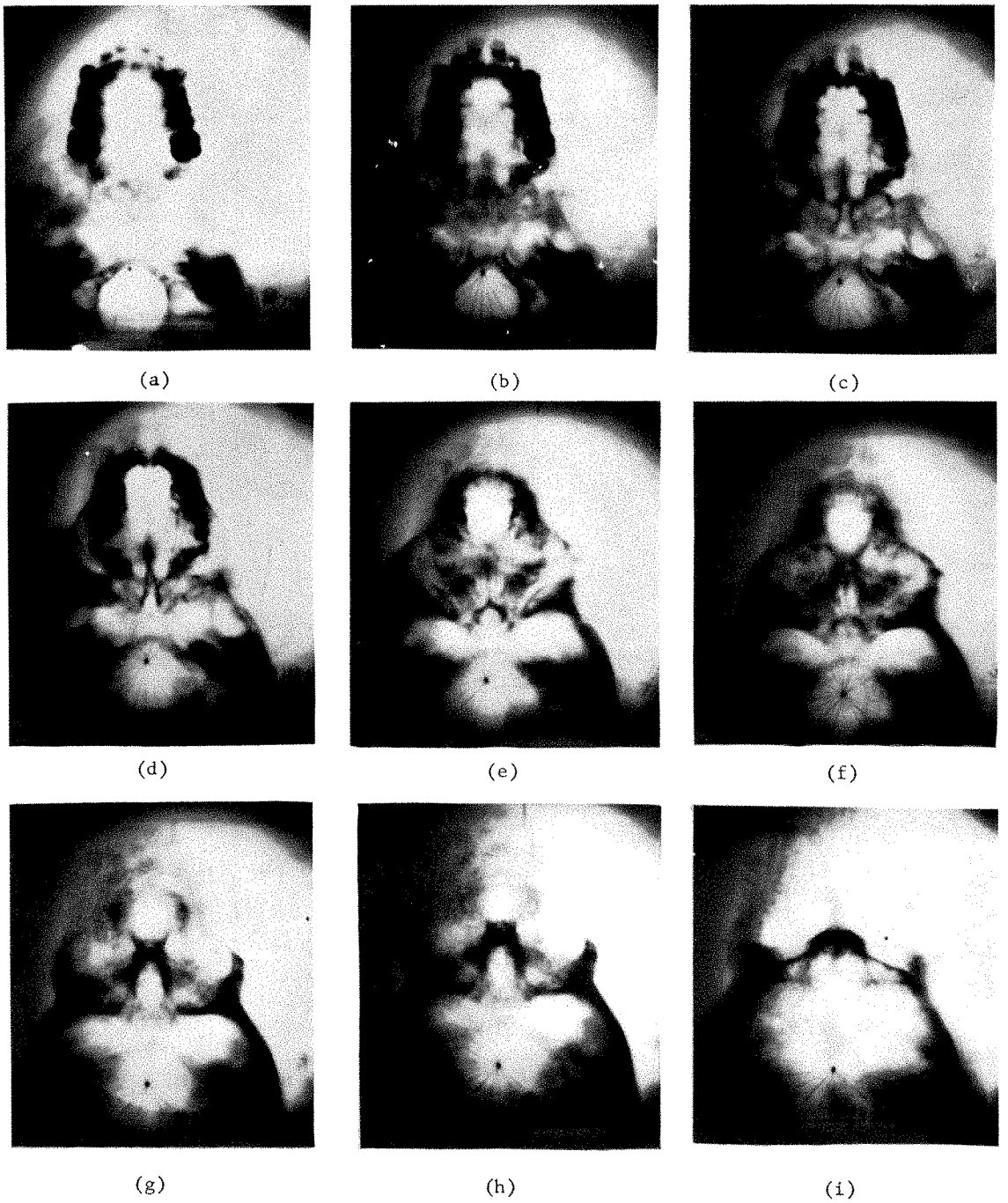


FIG. 7. (*a–i*) Roentgenograms of reconstructed chimpanzee skull.

DISCUSSION

The resolution of the present apparatus is not as good as that obtainable with conventional hypocycloidal tomography. The limitations, however, are known to be of a technical nature (*e.g.*, improved resolution of the wide angle lens near the edge of the field) and are not fundamental. As additional engineering improvements are made the resolution is expected to even-

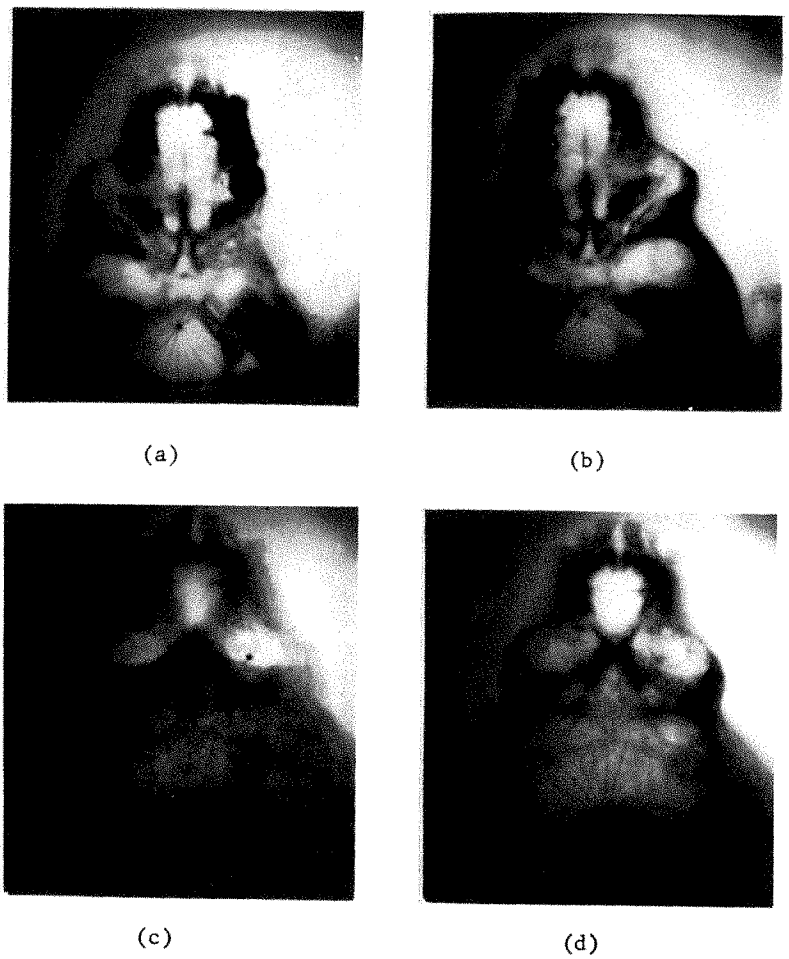


FIG. 8. (*a–d*) Roentgenograms of chimpanzee skull with rotated planes.

tually equal and, in certain situations, surpass (through judicious elimination of low contrast views) the resolution of standard tomography.

Work is continuing to adapt this technique for routine clinical use with the dual objective of reducing the roentgen-ray dosage and improving the resolution of normal tomography. A theoretical analysis has shown that the effects of "out of focus" objects which limit the performance of tomography can be greatly reduced by appropriate processing.

SUMMARY

A technique for producing a three-dimensional image of an object from a set of roentgenograms has been demonstrated. *N* individual roentgenograms, taken from different directions, are combined in a simple optical system producing a real image of the object in space. A moveable viewing screen permits observation of that part of the total image which corresponds to the roentgenogram of the thin section defined by the position of the screen.

David G. Grant
The Johns Hopkins University
Applied Physics Laboratory
8621 Georgia Avenue
Silver Spring, Maryland 20910

Technical assistance was provided by Miss M. Dubrosky, G. S. Bittings, C. R. Flick and J. E. Marrow.

VOL. 105, NO. 4

THE LINE SPREAD-FUNCTION AND THE MODULATION TRANSFER FUNCTION OF X-RAY FLUORESCENT SCREEN-FILM SYSTEMS—PROBLEMS WITH DOUBLE-COATED FILMS*

By G. LUBBERTS, M.S.
ROCHESTER, NEW YORK

AN IMAGE-FORMING system commonly used in medical radiography consists of a pair of fluorescent intensifying screens in contact with each side of a radiographic film. The film has a photographic emulsion coated on both sides of the support or base. When x rays are absorbed in the screens, light is emitted which, in turn, exposes the film. A method of measuring the spreading of light in screen–film systems is to excite the screen–film system with a narrow beam or "line" of x rays formed by a slit.[7,8] The slit used in this investigation is 12 microns wide and is formed by platinum jaws, 2 mm. thick. The apparatus for making such slit exposures is shown in Figure 1. The relative illuminance distribution in the film has been called the line spread-function (LSF) of the screen–film system.[8] A similar method has been employed by Morgan, Bates, Gopala Rao and Marinaro.[3]

The LSF is obtained by photographic photometry of the distribution of optical density in the double-coated film. The relative illuminance distribution is determined from the density distribution by means of wide-step sensitometry. In this manner, the screen–film system is "linearized." Röhler[5] and Doi[1] have pointed out that this approach is not valid, in general, because the relation between optical density and exposure is not uniquely defined when double-coated films are considered. Doi[1] defined the LSF of a screen–film system as an additive combination of the spatial distributions of illuminance in both emulsions which are obtained when the system is exposed to a long, but narrow, beam of x rays. Both methods of measuring the LSF will be examined and compared in this paper.

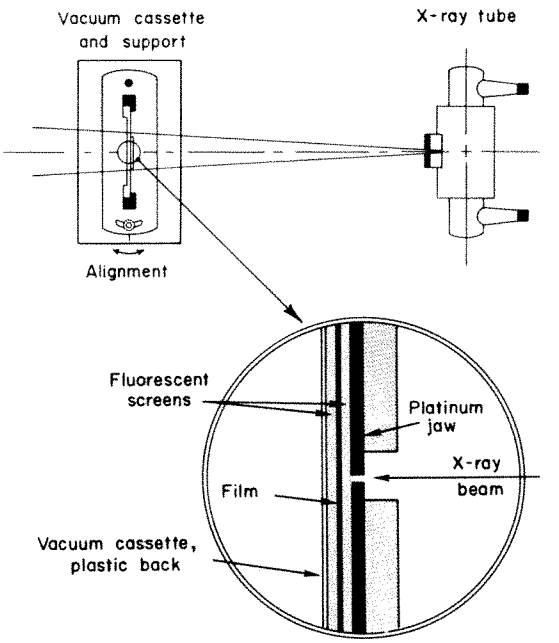


FIG. 1. Apparatus for making x-ray slit exposures.

SCREEN–FILM COMBINATION AS A LINEAR SYSTEM

Present medical x-ray films have like emulsion layers on each side of the base. Films with different emulsion layers on each side of the base are not considered in this paper. In this investigation of screen–film combinations with like emulsion layers, a distinction is made between symmetric and asymmetric screen–film systems. A symmetric screen–film system is one in which the spatial distribution (but not necessarily magnitude) of illuminance is the same in the two emulsions;

* From the Research Laboratories, Eastman Kodak Company, Rochester, New York.

asymmetric screen–film systems have different spatial distributions of illuminance in the two emulsions. For symmetric as well as asymmetric systems, a part of the light originating in one screen will be transmitted by the adjacent emulsion and expose the emulsion on the opposite side of the support. In spite of this crossover phenomenon, one can consider the slit images on both emulsions separately and write the total illuminance distribution in the film as

$$L_t(x) = L_f(x) + L_b(x), \qquad (1)$$

where

$L_f(x)$ is the relative illuminance in the front emulsion as a function of distance x.

$L_b(x)$ is the spatial distribution of illuminance in the back emulsion.

$L_t(x)$ is the spatial distribution of illuminance in the film which consists of two emulsions.

Both $L_f(x)$ and $L_b(x)$ can be measured by scanning slit images in the front and back emulsion* separately with a microdensitometer and relating optical density to relative exposure and therefore to relative illuminance by means of wide-step sensitometry. In the center of the slit image, $L_t(x)$ is normalized to unity.

Any image pattern on the film can be obtained, in principle, by convoluting the radiation pattern incident on the screen–film system with the (point or line) spread-function, when the conditions of linearity and spatial invariance are fulfilled. Linear in this context means that if an x-ray input, $H_i(x, y)$ produces a light output, $G_i(x, y)$, then the input:

$$H(x, y) = C_1H_1(x, y) + C_2H_2(x, y)$$

produces the output:

$$G(x, y) = C_1G_1(x, y) + C_2G_2(x, y),$$

where the x, y coordinates specify the position in the screen–film plane and C_1 and C_2 are arbitrary constants; that is, the addition of two inputs results in the addition of their outputs, and doubling one input, for example, doubles the corresponding output. Thus, linearity implies more than proportionality. It implies superposability of causes and superposability of their effects; *i.e.*, x-ray intensities as well as light intensities are additive.

The screen–film system itself can be considered as *spatially invariant.* That is, if an x ray input, $H(x, y)$, produces a light output, $G(x, y)$, then the x-ray input, $H(x+\xi, y+\eta)$, produces the light output, $G(x+\xi, y+\eta)$. In other words, the light-diffusion characteristics of the screen–film system are the same over the area of the screen–film system.

When the conditions of linearity and spatial invariance are not fulfilled, simple convolution procedures cannot be applied. Strictly speaking, linearity applies when the x-radiation is normally incident on the screen–film system, when the x-ray input is specified in terms of the absorbed x-ray energy pattern in the fluorescent screens used, when the intrinsic efficiency of the phosphor is not a function of x-ray energy over the energy range of interest, and when the spread function is independent of x-ray energy in the energy range of interest.

The spectral composition of the x-ray beam which emerges from an object and is incident on the screen–film system varies, in general, from point to point over the area of the screen–film system and can introduce a change in the spread function. However, the spread function is nearly independent of the quality of the x-ray beam for the kilovoltage range normally used in medical radiography.[7]

It appears that the measurement of an x-ray input presents a difficult task when the x-ray input is specified in terms of the x-ray energy absorbed in the screens. Since

* The spread function corresponding to one emulsion of the double-coated film describes the lateral spread of light in the emulsion plane when the source is a narrow beam of x rays incident on the screen–film system. The emulsion is not a plane, but is three-dimensional since it has thickness. Hence, the spread function is an "effective" spread function obtained by averaging throughout the depth of the emulsion. For simplicity, the word "effective" is deleted in the paper.

recorders differ in their spectral response, it is not proper to use just any recorder to measure the spatial x-ray input. The recorder should display the same spectral response as the film–screen system.

The condition of spatial invariance may be violated when scattered radiation is present in the x-ray input pattern. In practice, scattered radiation is incident on the screen–film system at a wide range of angles and the (point or line) spread-function measurements are made with a narrow beam of x rays normally incident on the screen–film system. Thus, it is not always a simple matter to relate the spatial input and output patterns by means of the conventional spread function, so that convolution procedures may break down.

Despite these possible problems, the LSF is a useful way for describing the light-diffusion characteristics of the screen–film system.

LINE SPREAD-FUNCTION MEASUREMENTS

I. SYMMETRIC SCREEN–FILM SYSTEMS

The magnitude as well as the spatial distribution of illuminance is essentially the same in the front and the back emulsion for many screen–film systems. This is the case when front and back screen are essentially identical and the absorption of x rays in a screen is small. Under these conditions, one expects that the LSF obtained by treating the double-coated film as a unit is identical to the evaluation of the distribution of illuminance on each emulsion and adding the results, as in Equation 1. To illustrate this point, Kodak Blue Brand Medical X-ray Film was exposed with a pair of medium-speed fluorescent screens to a beam of x rays which passed through a 12 micron-wide slit. In this and all subsequent experiments, the slit exposures were made with 70 kvp. x rays filtered by 0.25 mm. of copper at the tube (half-value layer of 3.4 mm. Al), and only calcium tungstate fluorescent screens were used.

The slit images on both emulsions were scanned separately with a microdensitometer. The characteristic curve (D-log E) of one emulsion was used to relate density to relative exposure and therefore to relative illuminance. The slit image and wide-step sensitometric results were obtained for each emulsion by removing the opposite emulsion chemically after the processed film had dried. In order to measure the LSF to low levels of illuminance, low-level and high-level slit exposures were made.[6] A low-level exposure was made for the evaluation of the maximum and near-maximum values of the LSF and a high-level exposure for evaluation of the tails of the LSF. A single LSF is constructed from these two slit exposures by means of the ratio of the two exposure levels. The maximum density in the slit image of the low-level exposure on double-coated film is between 1.70 and 2.00 for all screen–film systems under investigation.

Figure 2, Curves A and B, shows the illuminance distribution for front and back emulsion, respectively. The sum of these illuminance distributions is the total LSF,* $L_t(x)$, of the screen–film system and is illustrated in Figure 2, Curve C. In addition, the spatial illuminance distribution was obtained by scanning the slit image on the double-coated film (Fig. 2, Curve D). For the slit images as well as wide-step sensitometry, both emulsions were kept in focus during the scanning. As expected, Curves C and D in Figure 2 are essentially the same. The differences are probably within the limits of experimental error. This implies that the LSF of symmetric screen–film systems can be obtained with reasonable accuracy by scanning the slit image on the double-coated film.

II. ASYMMETRIC SCREEN–FILM SYSTEMS

In some practical screen–film systems, the phosphor layer of the back screen is thicker than that of the front screen. (The front screen is the first screen to be penetrated by the incident x-ray beam.) Such

* Since the LSF's are symmetric, only one-half of each function is shown.

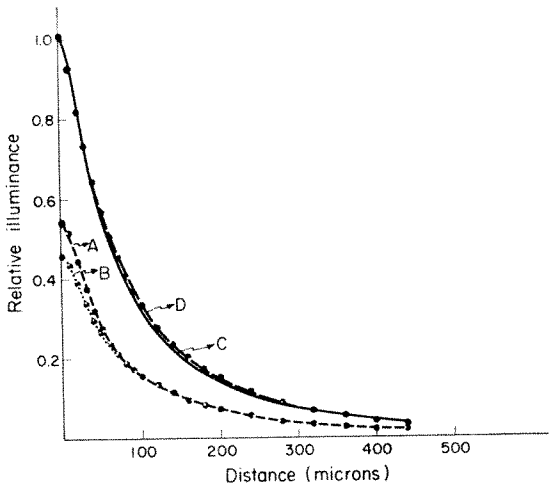


FIG. 2. Line spread-functions (LSF) for a symmetric screen–film system consisting of Kodak Blue Brand Medical X-ray Film and two medium-speed screens.

A. Illuminance distribution in front emulsion—$L_f(x)$.
B. Illuminance distribution in back emulsion—$L_b(x)$.
C. LSF of screen–film system obtained by addition of Curves A and B.
D. LSF of screen–film system obtained by treating double-coated film as a unit.

systems are expected to yield different slit images on the front and the back emulsion. Since a variety of such screen pairs exist, it seemed appropriate to investigate a few screen–film systems of pronounced asymmetry and study their LSF's. Previously, the LSF of a symmetric screen–film system was measured. The system consisted of Blue Brand Film sandwiched between medium-speed screens. To make this system artificially asymmetric, a Kodak Wratten Filter No. 0 (undyed gelatin) was placed between the back screen and the back emulsion to act as a separator. The transmission of this filter is about 90 per cent and is independent of wavelength over the emission spectrum of calcium tungstate screens. The thickness of this filter is approximately 100 microns. When slit exposures are made with this asymmetric system, the images on the front and the back emulsion are dissimilar. The spatial illuminance distribution in the front and back emulsion is shown in Figure 3, Curves A and B, respectively. The sum of these spatial illuminance distributions gives the total illuminance distribution of the screen–film system (Fig. 3, Curve C). Figure 3, Curve D, is obtained when the double-coated film is treated as a unit. Comparison of Curves C and D in Figure 3 shows that, in this case, the two methods do not yield exactly the same LSF, but again the differences are probably within the limits of experimental error.

A problem encountered in measurement with this particular asymmetric screen–film system deserves mention. In medical radiography with fluorescent screens, most of the exposure on the film is provided by light; only about 1 to 4 per cent of the total exposure on the film is due to direct x rays which are absorbed in the film. However, when screen–film systems are exposed to x rays passing through a narrow slit, a large proportion of the screen light

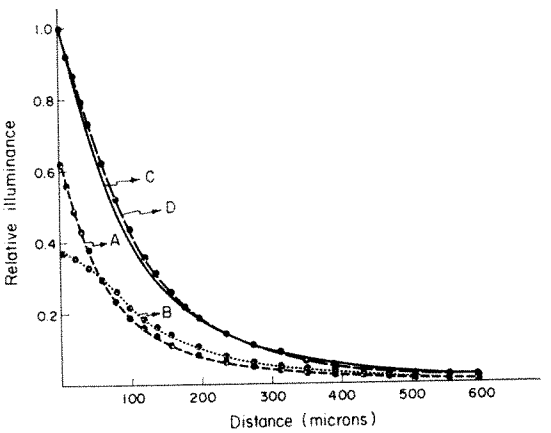


FIG. 3. Line spread-functions (LSF) for an asymmetric screen–film system consisting of Kodak Blue Brand Medical X-ray Film and two medium-speed screens. A Kodak Wratten Filter No. 0 was placed between back screen and back emulsion.

A. Illuminance distribution in front emulsion—$L_f(x)$.
B. Illuminance distribution in back emulsion—$L_b(x)$.
C. LSF of screen–film system obtained by addition of Curves A and B.
D. LSF of screen–film system obtained by treating double-coated film as a unit.

diffuses out of the slit region, but the direct x rays which penetrate the front screen are not scattered appreciably. Thus, they remain in the slit region so that the ratio of light exposure to x-ray exposure in the slit area becomes small.

In investigations of conventional screen–film systems, the use of a 12 micron-wide slit does not usually appear to cause an increase in density in the center of the slit image which can be attributed to direct x-ray exposure. However, the introduction of a 100 micron-thick separator between the back emulsion and the back screen makes the slit image on the back emulsion sufficiently unsharp so that a direct x-ray component is discernible. The slit image on the back emulsion showed a small, but sharp, peak superimposed on the unsharp spatial distribution of optical density. The effect of this sharp peak was excluded from the LSF determination. The density increase caused by the direct x-ray exposure is quite small; and when both emulsions were scanned together, the effect was neglected.

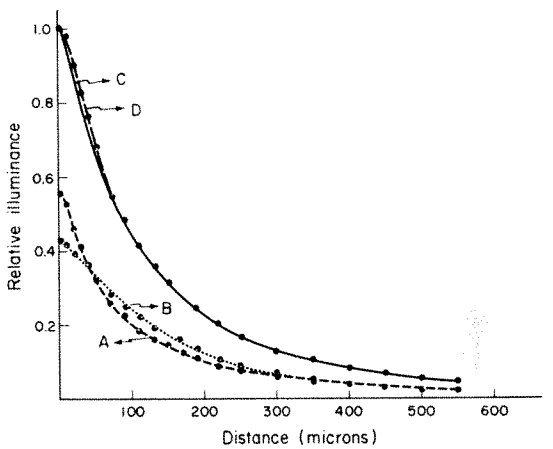


FIG. 4. Line spread-function (LSF) for an asymmetric screen–film system consisting of Kodak Royal Blue Medical X-ray Film, exposed with a medium-speed front screen and a fast back screen.
A. Illuminance distribution in front emulsion—$L_f(x)$.
B. Illuminance distribution in back emulsion—$L_b(x)$.
C. LSF of screen–film system obtained by addition of Curves A and B.
D. LSF of screen–film system obtained by treating double-coated film as a unit.

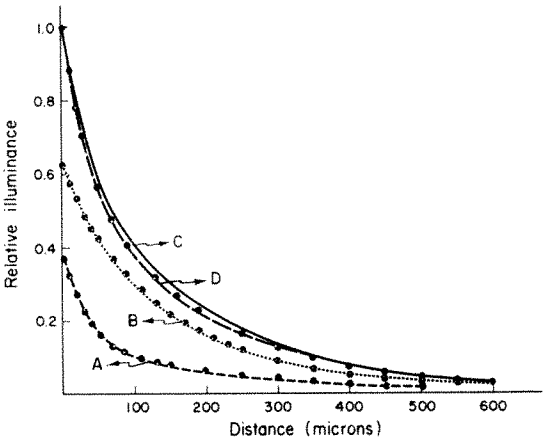


FIG. 5. Line spread-function (LSF) for an asymmetric screen–film system consisting of Kodak Blue Brand Medical X-ray Film, exposed with a slow front screen and a fast back screen.
A. Illuminance distribution in front emulsion—$L_f(x)$.
B. Illuminance distribution in back emulsion—$L_b(x)$.
C. LSF of screen–film system obtained by addition of Curves A and B.
D. LSF of screen–film system obtained by treating double-coated film as a unit.

Two additional asymmetric screen–film systems were considered. One of these systems consisted of Kodak Royal Blue Medical X-ray Film, exposed with a medium-speed front screen and a fast back screen. The LSF's corresponding to the front emulsion and the back emulsion are shown in Figure 4, Curves A and B, respectively. The LSF of the system, as defined by Equation 1, is given in Figure 4, Curve C, whereas Curve D is obtained when the double-coated film is treated as a unit. Only minor differences exist between Curves C and D and are probably within the limits of experimental error. The other screen–film system was extremely asymmetric and consisted of Blue Brand Film, exposed with a slow front screen and a fast back screen. The LSF's are shown in Figure 5. The small difference between Curves C and D of Figure 5 is somewhat larger than that expected from experimental error.

The difference between Curves C and D of Figure 5 might have occurred in the LSF evaluation if the microdensitometer did not sum correctly the densities on each emulsion in the slit image on a point-by-point basis. To test for this type of error in microdensitometry, the spatial density distributions on each emulsion of the slit image and on the sensitometric strips were added numerically for the asymmetric system shown in Figure 5. To obtain the "LSF" of the screen–film system, the numerically summed densities were related to relative illuminance. This procedure led to an "LSF" which was the same as that found by scanning both emulsions simultaneously (Curve D of Fig. 5). This test gives a reasonable indication that the microdensitometer has not introduced errors in the scanning of the slit images on double-coated films and that the small difference between Curves C and D of Figure 5 is real. The reason for this small difference between Curves C and D will be discussed in the following section.

ILLUMINANCE AND DENSITY DISTRIBUTION

The developed density of a film is not proportional to (light) exposure, so that the sum of densities of the front and the back emulsion is not proportional to the sum of exposures in the front and the back emulsion. It is this (non-linear) property of film that causes a distinction between symmetric and asymmetric screen–film systems as far as the LSF measurements are concerned.

For symmetric screen–film systems, the illuminance in the slit image has the same distribution in the front and the back emulsion and consequently the point-by-point ratio of the illuminances in the two emulsions is constant. For such systems, wide-step sensitometry produces the same ratio of illuminances in the two emulsions as slit exposures. Therefore, the density in the slit image on double-coated film can be related to relative illuminance since the illuminance ratios are the same, that is, the density contributions from the front and the back emulsion are the same for the slit image as the sensitometric exposure. Thus, the LSF's of symmetric screen–film systems can be evaluated by treating the double-coated film as a unit, even though, in general, density is not proportional to exposure.

For asymmetric screen–film systems, however, the spatial distribution of illuminance in the slit image is different in the two emulsions. This means that the ratio of illuminance in the back emulsion to that in the front emulsion is *not constant* but a function of the distance across the slit image. (See, for example, Fig. 6, to be discussed later.) However, for wide-step sensitometry the ratio of illuminance in the back emulsion to that in the front emulsion is *constant*. Consider, for instance, any point in the slit image at which the ratio of illuminance in the front emulsion to that in the back is different from the ratio for wide-step sensitometry. The total density at such a point in the slit image is made up of densities in the front and the back emulsions. In general, these densities differ from the densities in the front and the back emulsions of a sensitometric exposure that produces the same total density. Although the sums of densities are equal, the

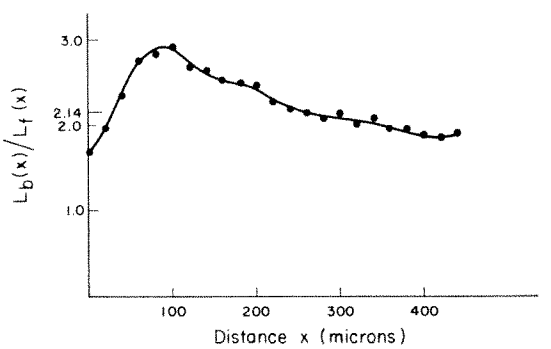


FIG. 6. Ratio of illuminance distribution in back emulsion to that in front emulsion, $L_b(x)/L_f(x)$, for an asymmetric screen–film system. (Ratio of Curves B and A in Fig. 5.) The value of 2.14 on the ordinate corresponds to the ratio of exposures of back to that of front emulsion for large-area exposures.

sums of exposures are not because density is not proportional to exposure. Therefore, the slit density cannot be related to exposure when the illuminance ratios are different, that is, when the density contributions from front and back emulsions of the slit image are not the same as those of the sensitometric densities. For these reasons, the D-log E (characteristic) curve obtained from wide-step exposures cannot be used to relate density to exposure in the slit image of asymmetric screen–film systems when the double-coated film is treated as a unit. In fact, there is no single D-log E curve of a double-coated film that can be used for this purpose.

Were density proportional to exposure, the double-coated film method could be applied to asymmetric (as well as to symmetric) screen–film systems, provided the film had like emulsion layers on each side of the base. In such an idealized case, the sum of the densities in the front and the back emulsion would also be proportional to the sum of the exposures in the front and the back emulsion. However, if density were proportional to exposure, it would not be necessary to obtain a D-log E curve, since the screen–film system would be linear.

To be more specific, let us consider the extremely asymmetric screen–film system which was analyzed previously (Fig. 5). This system consisted of Blue Brand Film, exposed with a slow front screen and a fast back screen. The spatial illuminance distribution in the front and the back emulsion is shown in Figure 5, Curves A and B. The ratio, $L_b(x)/L_f(x)$, of the illuminance distribution in the back to that in the front emulsion is shown in Figure 6. The ratio of illuminances in the back and the front emulsion for large-area exposures (wide-step sensitometry) is 2.14 for this system. Clearly, in general, wide-step sensitometry cannot be used when the LSF is evaluated by treating the double-coated film as a unit.

When the LSF of asymmetric screen–film systems is determined by treating the double-coated film as a unit, it is likely that different results will be obtained when either the density level in the slit image or the shape of the D-log E curve of the film or both are changed, all other factors being constant.

The reasonable agreement between Curves C and D of Figures 3, 4, and 5 is attributed to the fact that the gross density (*i.e.*, total density including base density) was nearly proportional to exposure over a considerable range of exposures, in these particular cases. By means of convolution procedures Rossmann and Sanderson[9] also have shown that the line spread-function for present asymmetric screen–film systems can be obtained with reasonable accuracy by treating the double-coated film as a unit.

OPTICAL TRANSFER FUNCTION

A discussion of the LSF of screen–film systems naturally leads to the optical transfer function (OTF). The OTF of a linear, spatially invariant, image-forming system is defined as the ratio of Fourier transforms of image and object intensity patterns.[4] Frequently, the OTF of an image-forming system is obtained by means of a radiation pattern in which intensity varies sinusoidally with distance in one dimension. Unfortunately, it is difficult to obtain a spatial, sinusoidally varying, x-ray intensity distribution. An indirect method of measuring the OTF is to irradiate the fluorescent screen–film system with a beam of x rays which passes through a narrow slit.[3,7,8] The Fourier transform of the resulting illuminance distribution in the film (LSF) is the OTF. The modulus or magnitude of the OTF is the modulation transfer function* (MTF). For screen-film systems the OTF is real and positive and consequently equal to the MTF. The MTF is then obtained by taking the Fourier transform of both sides in Equation 1. Rewriting Equation 1 yields

* This terminology is in agreement with the recommendations formulated by the Subcommittee for Image Assessment Problems of the International Commission for Optics.[2]

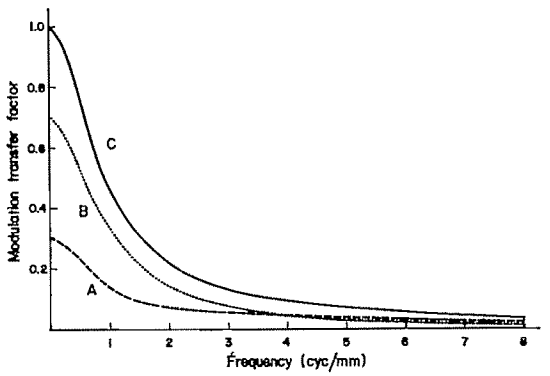


FIG. 7. Modulation transfer functions (MTF) for an asymmetric screen–film system consisting of Kodak Blue Brand Medical X-ray Film, exposed with a slow front screen and a fast back screen.
A. MTF associated with illuminance distribution, $L_f(x)$, in front emulsion—0.3 $M_f(\nu)$.
B. MTF associated with illuminance distribution, $L_b(x)$, in back emulsion—0.7 $M_b(\nu)$.
C. MTF of screen–film system obtained by addition of Curves A and B.

$$E_t \frac{L_t(x)}{E_t} = E_b \frac{L_b(x)}{E_b} + E_f \frac{L_f(x)}{E_f}, \quad (2)$$

where

$$E_f = \int_{-\infty}^{\infty} L_f(x)dx,$$

$$E_b = \int_{-\infty}^{\infty} L_b(x)dx, \quad (3)$$

$$E_t = E_f + E_b.$$

Taking the Fourier transform of both sides of Equation 2, we obtain

$$E_t M_t(\nu) = E_b M_b(\nu) + E_f M_f(\nu), \quad (4)$$

where $M_f(\nu)$, $M_b(\nu)$, and $M_t(\nu)$ are the modulation transfer functions derived from the illuminance distribution in the front emulsion, the back emulsion, and the total system, respectively; ν denotes the spatial frequency. The reason for rewriting Equation 1 in the form of Equation 2 is to make all MTF's in Equation 4 unity for zero spatial frequency. Upon dividing both sides of Equation 4 by E_t and setting $k = E_b/E_t$, we get

$$M_t(\nu) = kM_b(\nu) + (1 - k)M_f(\nu). \quad (5)$$

The MTF's corresponding to the front and the back emulsion were obtained for the asymmetric screen–film system which consisted of Blue Brand Film, exposed with a slow front screen and a fast back screen (Fig. 5). For this system a value of 0.70 was obtained for k by computing the areas under the illuminance distribution curves for front and back emulsion which are shown in Figure 5, Curves A and B. Also, k can be obtained from the ratio of exposures in front and back emulsion by use of wide-step sensitometry, since k can be written as

$$k = \frac{1}{1 + E_f/E_b}. \quad (6)$$

In the latter case, a value of $k = 0.68$ was obtained which agrees remarkably well with the previous value of 0.70. The total MTF, $M_t(\nu)$, as well as the MTF's corresponding to front and back emulsion are shown in Figure 7. Thus, the MTF of an asymmetric screen–film system can be measured from the sum of weighted MTF's derived from the illuminance distribution in the front and the back emulsion (Equation 5). The weighting factors are the ratios of the light exposure in each of the two emulsions to the total light exposure produced by a uniform x-ray exposure.

SUMMARY

The line spread-function (LSF) of the screen–film system has been defined as the sum of the spatial distribution of illuminance in the front and the back emulsion caused by a beam of x rays which passes through a narrow slit. Fourier transformation of the LSF gives the corresponding modulation transfer function (MTF).

In the past, the LSF has been obtained by scanning slit images on double-coated film. This method can be justified for symmetric screen–film systems, but is, in general, invalid for asymmetric screen–film systems, although the errors introduced may be small, even for grossly asymmetric systems, as is shown in this paper. In practice, many screen–film sys-

tems are essentially symmetric and yield nearly the same LSF's and MTF's by either method. For this reason, it is valid to obtain the LSF and MTF of such systems by treating the double-coated film as a unit. A mathematical analysis indicates that the MTF of the screen–film system is the sum of weighted MTF's derived from the illuminance distribution in the front and the back emulsion. The weighting factors are the ratios of the light exposure in each of the two emulsions to the total light exposure produced by a uniform x-ray exposure.

Research Laboratories
Eastman Kodak Company
Rochester, New York 14650

The author is grateful to Mr. H. M. Cleare, of these Research Laboratories, for helpful discussions.

REFERENCES

1. Doi, K. Optical transfer function in radiography. IV. Combination of screen and film. *Oyo Buturi*, 1966, *35*, 559–664.
2. Ingelstam, E. Nomenclature for Fourier transforms of spread functions. *J. Optic. Soc. Am.*, 1961, *51*, 1441.
3. Morgan, R. H., Bates, L. M., Gopala Rao, U. V., and Marinaro, A. Frequency response characteristics of x-ray films and screens. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1964, *92*, 426–440.
4. Murata, K. Progress in Optics. Volume V. Edited by E. Wolf. North-Holland Publishing Company, Amsterdam, 1965, p. 201.
5. Röhler, R. Modulation transfer function of intensifying screens: problems of its definition and measurement. In: Diagnostic Radiologic Instrumentation: Modulation Transfer Function. Charles C Thomas, Publisher, Springfield, Ill., 1965, p. 110.
6. Rossmann, K. Measurement of modulation transfer function of radiographic systems containing fluorescent screens. *Phys. Med. & Biol.*, 1964, *9*, 551–557.
7. Rossmann, K., and Lubberts, G. Some characteristics of line spread-function and modulation transfer function of medical radiographic films and screen–film systems. *Radiology*, 1966, *86*, 235–241.
8. Rossmann, K., Lubberts, G., and Cleare, H. M. Measurement of line spread-function of radiographic systems containing fluorescent screens. *J. Optic. Soc. Am.*, 1964, *54*, 187–190.
9. Rossmann, K., and Sanderson, G. K. Validity of modulation transfer function of radiographic screen-film systems measured by slit method. *Phys. Med. & Biol.*, 1968, *13*, 259–268.

THE AMERICAN JOURNAL OF ROENTGENOLOGY RADIUM THERAPY AND NUCLEAR MEDICINE

Editor: TRAIAN LEUCUTIA, M.D.

Assistant to the Editor: KENNETH L. KRABBENHOFT, M.D.

Associate Editors: HARRY HAUSER, M.D., RUSSELL H. MORGAN, M.D., EDWARD B. D. NEUHAUSER, M.D.

Consulting Editorial Board: See front cover.

Published by: CHARLES C THOMAS, Publisher, 301–327 East Lawrence Avenue, Springfield, Illinois 62703.

Issued monthly. Annual subscription: United States, Mexico, Cuba, Central and South America, and Canada $20.00; other countries, $22.00. Current single numbers, $2.00. Advertising rates submitted on application. Editorial office, 401 Professional Building, Detroit, Michigan 48201. Office of publication, 301–327 East Lawrence Avenue, Springfield, Illinois 62703. Information of interest to authors and readers will be found on page ii.

AMERICAN ROENTGEN RAY SOCIETY

President: S. W. Brown, Augusta, Ga.; *President-Elect:* J. C. Cook, Detroit, Mich.; *1st Vice-President:* S. F. Ochsner, New Orleans, La.; *2nd Vice-President:* Herbert M. Stauffer, Philadelphia, Pa.; *Secretary:* T. F. Leigh, Emory University Clinic, Atlanta, Ga. 30322; *Treasurer:* C. B. Holman, Mayo Clinic, Rochester, Minn. 55901.

Executive Council: S. W. Brown, J. C. Cook, S. F. Ochsner, T. F. Leigh, C. B. Holman, T. M. Fullenlove, W. N. Hanafee, J. F. Roach, C. M. Nice, Jr., E. F. Lang, H. O. Peterson, C. A. Stevenson, C. A. Good, T. Leucutia, R. M. Scott, S. W. Nelson, R. L. Tondreau, W. B. Seaman, E. F. Van Epps, Chairman, Duke Univ., Durham, N. C., 27706.

Program Committee: T. F. Leigh, J. F. Roach, T. Leucutia, E. F. Lang, H. O. Peterson, W. N. Hanafee, S. W. Brown, E. F. Van Epps, J. C. Cook, Chairman, LL 14 Professional Plaza, 3790 Woodward Ave., Detroit, Mich. 48201.

Publication Committee: R. H. Greenspan, J. O. Reed, R. N. Cooley, P. A. Riemenschneider, J. F. Roach, Chairman, Albany, N. Y.

Finance and Budget Committee: R. L. Tondreau, W. B. Seaman, G. E. Sheline, J. M. Dennis, T. M. Fullenlove, Chairman, San Francisco, Calif.

Committee on Scientific Exhibits: R. E. Parks, R. G. Lester, W. N. Hanafee, Chairman, UCLA Medical Center, Los Angeles, Calif. 90024.

Advisory Committee on Education and Research: E. C. Klatte, A. R. Margulis, D. M. Witten, F. J. Bonte, C. M. Nice, Jr., Chairman, New Orleans, La.

Representatives on the American Board of Radiology: J. F. Roach, Albany, N. Y.; S. W. Nelson, Columbus, Ohio; and C. A. Stevenson, Spokane, Wash.

Director of Instruction Courses: H. O. Peterson, Minneapolis, Minn.; *Associate Director:* D. G. Mosser, Minneapolis, Minn.

Manager of the Annual Meeting: E. F. Lang, LL 14 Professional Plaza, 3790 Woodward Ave., Detroit, Mich. 48201.

Editor: T. Leucutia, 401 Professional Building, Detroit, Mich. 48201.

Representative on the Board of Chancellors of the American College of Radiology: S. F. Ochsner.

Seventieth Annual Meeting: Washington-Hilton Hotel, Washington, D. C., September 30–October 3, 1969.

AMERICAN RADIUM SOCIETY

President: Juan A. del Regato, Colorado Springs, Colo.; *President-Elect:* Fernando G. Bloedorn, Boston, Mass.; *1st Vice-President:* Clifford L. Ash, Toronto, Ont., Canada; *2nd Vice-President:* H. Peter Mueller, Boston, Mass.; *Secretary:* John V. Blady, The Parkway House, 2201 Benjamin Franklin Parkway, Philadelphia, Pa. 19130; *Treasurer:* James F. Nolan, 1407 South Hope St., Los Angeles, Calif. 90015.

Executive Committee: Justin J. Stein, Chairman, Los Angeles, Calif.; Juan A. del Regato; Fernando G. Bloedorn; Clifford L. Ash; H. Peter Mueller; John V. Blady; James F. Nolan; Milton Friedman; John L. Pool.

Scientific Program Committee: Juan A. del Regato, Chairman; Fernando G. Bloedorn, Vice-Chairman; Simon Kramer; Wm. E. Powers; Felix N. Rutledge; Jerome M. Vaeth.

Arrangements Committee: Luther W. Brady, Chairman, Philadelphia, Pa.; Gordon Verity, Chairman Designate; Larry McGowan; David Sklaroff; Antolin Raventos; James F. Nolan.

Publication Committee: Harry Hauser, Chairman, Cleveland, Ohio; Giulio J. d'Angio; William T. Moss.

Public Relations Committee: Antolin Raventos, Chairman; Robert Robbins; Harvey P. Groesbeck; Gordon Verity, *ex officio.*

Janeway Lecture Committee: Clifford L. Ash, Chairman, '69, Toronto, Ont., Canada; A. N. Arneson, '71; Milford D. Schulz, '73.

Representatives on the American Board of Radiology: Justin J. Stein, Los Angeles, Calif.; Ralph M. Scott, Louisville, Ky.; E. Richard King, Richmond, Va.

Liaison Representatives on the National Council on Radiation Protection and Measurements: Herbert M. Parker, Richland, Wash.; Marvin M. D. Williams, Rochester, Minn.

Representative on the Board of Chancellors of the American College of Radiology: Charles G. Stetson.

Fifty-first Annual Meeting: Bellevue Stratford Hotel, Philadelphia, Pa., April 28–30, 1969.

EDITORIALS

WINDS OF CHANGE PASS OVER THE A. U. R.

THE Association of University Radiologists (A. U. R.) began as a small group of full-time academic radiologists, meeting informally to share information, aspirations and friendships. Now, 16 years later, we are facing problems concerning size, character and goals which many of us hoped might never arise, but which are upon us and urgently demanding change.

The A. U. R. was born in May, 1953, at an organizational meeting in Chicago. Russell Morgan, Paul Hodges, Fred Hodges, Henry Kaplan, Hugh Wilson and George Ramsey were its prime movers. Twenty-eight members established its core, representing at first only the 6 universities in which these 6 men were Chairmen of Radiology Departments: Johns Hopkins, Chicago, Michigan, Stanford, Washington University and Rochester. By 1956 there were 83 members at 36 schools; and in 1969 there are 247 members at 71 medical schools.

Since its beginning, the goals of the A. U. R. have been: (1) to encourage laboratory and clinical investigation in radiology by the informal exchange of ideas; (2) to stimulate interest in academic radiology as a medical career; and (3) to advance radiology as a medical science. Simple as they are, and pertinent as they may seem to anyone interested in full-time academic radiology, these goals have occasioned much heated comment since 1953, from inside and outside our ranks.

Items of contention have been that: applicants for membership must be established full-time academic radiologists; they must suffer an evaluation of "academic quality" in order to be elected; our officers and standing committee members cannot be over 50 years of age; we talk too much at our meetings about basic research and not enough about clinical teaching and clinical practice; there are not enough radiotherapists active in the group; we do not maintain a permanent administrative structure to exert influence in our behalf, or even an opposite view that radiology doesn't need another national organization.

This year A. U. R. is engaged in a re-evaluation of its aims and constitution. I cannot report results yet but there is every likelihood that it will seek a more inclusive membership, still from the ranks of full-time academic people in all branches of the radiological sciences, still likely stressing youth and informality, but probably with a more balanced view on elements of teaching, research and clinical work. And it will very likely seek an increasing representative role in radiological affairs.

Full-time academic radiologists are, of course, a minority of all radiologists, although our numbers are increasing relatively and absolutely. Only 9.7 per cent of the total pool of board-certified radiologists are full-time American university faculty members.[1] We have varying but intense degrees of involvement in teaching, research, administration or clinical practice, as indeed do other radiologists outside of universities.

However, I believe that most of us work within universities because we find them the most fruitful ground for fulfilling such a variety of interests. Also, we are enticed and challenged by the concentration of talents throughout medical schools, in-

[1] Personal communication from Steven Ross, M.D., Department of Radiology, University of California Medical Center, San Francisco. Dr. Ross points out, however, that 9.7 per cent ranks third highest among all specialties.

cluding students and house officers. Because of the economics of medical schools, those who enjoy or endure the environment tend to be talented at suppressing our natural craving for maximal income. And finally, because of the institutional structure, we are forced to accept less than maximal personal and professional independence.

Various trends—social, educational, professional and economic—are focusing inincreasing attention on this academic minority. The potentially pervasive Regional Medical Programs are, by legislative *fiat*, supposed to bear our professional, academic and administrative stamps in our localities, often including a strong commitment of time and radiological services. Community Health Centers, developing under various programs to conquer social inequity, are pleading for similar commitment. Not in all, but in many communities, our primary university hospitals tend to be the dominant meccas for health care of all types, by popular selection, and their relative local service dominance is growing. For reasons of mutual advantage, other community hospitals are affiliating with us in rapidly increasing numbers and beginning to feel some measure of our administrative control.

In this matter of trends: in September, 1967, there were 2,340 approved residency positions offered in radiology in the United States, of which 80 per cent were in university or university-affiliated hospitals.[2] Five years before, in 1962, the respective figures were 1,972 and 73 per cent.[3] Certainly, not all the training or education of these house officers is done by full-time academic radiologists, but our administrative presence, whether domineering or mild, is quite palpable in all instances.

Thinking only of residency training, consider first that 9.7 per cent of all radiologists exercises considerable direct influence upon the training of 80 per cent of all radiology residents. Next, consider that many among this small group of academic radiologists might be expected to feel more kinship with the Association of American Medical Colleges (A.A.M.C.) as it reorganizes along lines suggested by its commendable Coggeshall Report,[4] than with the American Medical Association (A.M.A.) as it responds to its own commendable Millis Report.[5] Similar leanings may be suspected in other medical school departments as well, so that the summation of the trend *might* be to strengthen the hand of the A.A.M.C. in directing residency programs, *vis-à-vis* the present dominant position of the A.M.A. (I do not mean to deprecate the great contribution of the A.M.A., which assumed this responsibility when nobody else wanted it. Nor am I ignoring the fact that the general public will merit a voice in what we do and how we are doing it.)

Naive as this Machiavellian musing may sound, coming from the transient, soon-to-be-over-50 President of only 247 academicians, it offers a hint of some new responsibilities lying in wait for us.

From the start, there has been no doubt that academic radiologists have sectarian, complex interests and problems which warrant an Association of University Radiologists and an annual meeting, even though we continue to be welcome in all other national radiological societies and meetings. Those societies have attempted to serve the needs of the entire profession and have been in many ways dynamic and sensitive to needs for change. By redefining our goals and constitution, we also hope to strengthen our own contribution to the medical community.

Stanley M. Rogoff, M.D.
President, Association of University Radiologists

Division of Diagnostic Radiology
University of Rochester Medical Center
Rochester, New York 14620

[2] Annual Report on Graduate Medical Education in the United States. *J.A.M.A.*, Nov. 25, 1968, *206*, pp 2032–2033.

[3] Graduate Medical Education. *J.A.M.A.*, 1963, *186*, p. 679.

[4] *Coggeshall, L. T.* Planning for Medical Progress through Education. Association of American Medical Colleges, Evanston, Ill., 1965.

[5] The Graduate Education of Physicians. American Medical Association, Chicago, Ill., 1967.



PALMER E. WIGBY, M.D.
1903-1968

DR. PALMER E. WIGBY, born in Antler, North Dakota, on August 28, 1903, a Houston radiologist for the past 27 years, died at St. Joseph's Hospital in Houston on November 16, 1968, following a short catastrophic illness.

Dr. Wigby was a former Chief of the Departments of Radiology at Parkland Hospital in Dallas and St. Joseph's Hospital in Houston. For the past several years he was engaged in the private practice of radiology at his office in the Hermann Professional Building of Houston. He served on the volunteer faculty of Baylor College of Medicine for 32 years as Instructor, Assistant Professor and Associate Professor.

Dr. Wigby received his M.D. degree from the University of Minnesota and his training in radiology at the University of Michigan Hospital in Ann Arbor. He was a Past President of the Texas Radiological Society.

Department of Radiology
The Methodist Hospital
Texas Medical Center
Houston, Texas 78025

Curtis H. Burge, M.D.

NEWS ITEMS

THE AMERICAN COLLEGE OF RADIOLOGY

The Forty-fifth Annual Meeting of the American College of Radiology was held at the Regency Hyatt House, Atlanta, Georgia, from Tuesday to Saturday, February 18–23, 1969.

The following officers were elected: *President*, J. Frank Walker, Atlanta, Georgia; *Vice-President*, John R. Danstrom, Oklahoma City, Oklahoma; *Secretary-Treasurer*, Karl C. Corley, Washington, D.C.; *Chairman, Board of Chancellors*, Robert W. McConnell, Dallas, Texas; *Vice-Chairman, Board of Chancellors*, Seymour F. Ochsner, New Orleans, Louisiana.

Dr. McConnell was re-elected to a second Board term, along with Dr. G. M. McDonnell of Los Angeles, California. Newly elected to the Board are Dr. John W. Beeler, Indianapolis, Indiana and Dr. George W. Satterwhite, Portland, Oregon.

Thursday evening, the Joint Dinner with the ACR-Georgia Chapter, was addressed by Wallace S. Sayre, Ph.D., LL.B., Columbia University, New York, on the "Political Dynamics of Government Health Policies."

The College Fellowship Convocation was held Friday, at 5:30 P.M., with Dr. Joseph D. Calhoun, President of the American College of Radiology, presiding. The degree of Fellow of the American College of Radiology was conferred on 122 candidates, and of Fellow in Physics on 3 candidates, the largest number ever approved in a single year by the Board of Chancellors and elected to fellowship by the vote of the Fellows.

The degree of Honorary Fellow was awarded to Dr. F. Mason Sones, Jr., Cleveland, Ohio; Dr. Ronald O. Murray, London, England; and Dr. Armin Schwartz, Jerusalem, Israel.

Gold Medals, the highest award of the American College of Radiology "for distinguished service to radiology," were conferred to: Dr. Richard H. Chamberlain, Philadelphia, Pennsylvania; Dr. Philip J. Hodes, Philadelphia, Pennsylvania; and Dr. Theodore J. Wachowski, Wheaton, Illinois.

On Saturday, Dr. Benjamin Felson, Cincinnati, Ohio, Chairman of the Commission on Education, had arranged an extremely interesting and very timely program for the Teachers' Conference, which is always, an important part of the meeting.

The Forty-sixth Annual Meeting of the American College of Radiology will be held at the Statler-Hilton Hotel, Dallas, Texas, March 31-April 4, 1970.

SOUTHERN RADIOLOGICAL CONFERENCE

At the Thirteenth Annual Meeting of the Southern Radiological Conference, held at the Grand Hotel, Point Clear, Alabama, January 31, February 1 and 2, 1969, the following new officers were elected: *Chairman*, Dr. Buell C. Buchtel, Foundation Hospital, 1516 Jefferson Highway, New Orleans, Louisiana 70121; *Vice-Chairman*, Dr. Allan E. Green, Jr., 865 Jefferson Avenue, Memphis, Tennessee 38103; and *Secretary-Treasurer*, Dr. Marshall Eskridge, Mobile Infirmary, P.O. Box 4097, Alabama 36604 (re-elected).

The Fourteenth Annual Meeting will be held at the Grand Hotel, Point Clear, Alabama, January 30, 31 and February 1, 1970.

AMERICAN SOCIETY OF CYTOLOGY

The Seventeenth Annual Meeting of American Society of Cytology will be held at the Palmer House, Chicago, Illinois, November 6–8, 1969.

For information, contact Warren R. Lang, M.D., Secretary-Treasurer, 7112 Lincoln Drive, Philadelphia, Pennsylvania 19119.

WORLD CONGRESS ON ULTRASONIC DIAGNOSTICS IN MEDICINE

An International Congress on Ultrasonic Diagnostics will be held in Vienna, June 2–7, 1969.

The organizers are: Various departments of the University of Vienna Hospitals; Societas Internationalis de Diagnostica Ul-

trasonica in Ophthalmologia (SIDUO); and American Institute of Ultrasonics in Medicine (AIUM).

The subjects to be discussed include: Ultrasonic diagnostics in all medical disciplines; technology and methods; experimental and clinical experience; and standardization.

Inquiries, registrations, and requests for programs should be directed to Dr. K. Ossoinig, Vienna Academy of Medicine, Stadiongasse 6–8, A-1010 Vienna, Austria.

AMERICAN INSTITUTE OF ULTRASOUND IN MEDICINE (AIUM)

The Fourteenth Annual Conference of the American Institute of Ultrasound in Medicine will be held at the Hotel Fort Gary, Winnipeg, Manitoba, Canada, October 6–10, 1969.

The topics include: (1) a two day diagnostic workshop with basic principles, intended for those newly acquainted with ultrasound or those wishing a refresher course in the diagnostic applications of ultrasound; and (2) a two and a half day scientific session.

Scientific papers are solicited on the clinical applications and developments in technique and instrumentation of diagnostic, therapeutic and surgical ultrasound.

Four hundred (400) word *abstracts*, including figures, should be sent by June, 30, 1969 to: Ross E. Brown, M.D., Program Chairman, AIUM, Department of Continuing Medical Education, 15 Medical College Building, Bannatyne & Emily Streets, Winnipeg 3, Manitoba, Canada.

Abstracts will be published as proceedings of the meeting and will be distributed at the meeting.

EUROPEAN "SOCIETY OF NUCLEAR MEDICINE"

George von Hevesy Prize

At the Annual Meeting of the European "Society of Nuclear Medicine" to be held in Zurich, September 25–27, 1969, the George von Hevesy Prize will be awarded for the first time. The prize amounts to the sum of US-Dollar 1,250.

Unpublished scientific papers in English or German on the subject of Nuclear Medicine can be submitted by authors who are not more than 40 years of age. The papers should not be longer than 12 typewritten pages. Upon decision of the Committee of Trustees the prize can be split.

The manuscripts should be sent by June 30, 1969, to the President of the European "Society of Nuclear Medicine," Prof. Dr. W. Horst, Clinic of Nuclear Medicine, University of Zurich, Rämistrasse 100, Zurich, Switzerland.

II REUNIÃO BRASILEIRA DE NEURORADIOLOGIA

In the May 1968 issue of this JOURNAL, it was announced that the Brazilian Society of Neuroradiology will hold the Second Reunion of Neuroradiology, at Rio de Janeiro, July 24–28, 1969.

Dr. A. Thomas Rezende, President of the Reunion, extends a most cordial invitation to the radiologists and associated scientists the world over to attend. An outstanding program has been arranged. There will be basic courses, lectures, presentation of free topics, scientific exhibition and two round-table discussions on "Scanning as a Contribution to Neuroradiology" and "The Teaching of Neuroradiology."

The opening ceremony will be held at the National Academy of Medicine on July 24, 1969 and the plenary sessions at the Copacabana Palace Hotel. Social activities are also scheduled for participants and their accompanying members.

Former Presidents of Symposia Neuroradiologica have been invited to take part as well as to present papers. Internationally famous colleagues were also invited to attend this meeting.

It is requested that application be made as soon as possible.

July is a very busy month in Rio de Janeiro (school holidays), and hotel accommodation must be secured quite some time in advance.

Application forms and further informa tion may be obtained by writing to Dr. Amarino C. Oliveira, the Secretary, Clínica Radiológica Emilio Amorim, ZC-02 rua Sorocaba, 464–1.º, Rio de Janeiro-Gb.

BOOKS RECEIVED

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the cortesy of the sender. Selections will be made for the interest of our readers as space permits.

Comparative Study of Roentgen Diagnostic Classifications: Computer Analysis of 124, 496 Roentgen Reports. By Erkki Koivisto, Department of Radiology, University of Oulu, Finland. Paper. Pp. 125, with some illustrations. Price, Sw. Kr. 35. Acta Radiologica Supplementum 285. Acta Radiologica, Stockholm 2, Sweden, 1969.

Results of Treatment of Slipped Upper Femoral Epiphysis: A Survey of 99 Treated Hips. By P. Salenius and R. Kivilaakso, the Orthopedic Hospital of the Invalid Foundation, Helsinki, Finland. Paper. Pp. 56, with some figures. Acta Orthopaedica Scandinavica Supplementum No. 114. Munksgaard, Copenhagen, 1968.

Growth in Length of Bones in Change of Oxygen and Carbon Dioxide Tensions. By Björn Mauritz Persson, Department of Orthopedic Surgery, University Hospital, Lund, Sweden. Paper. Pp. 100, with some tables. Acta Orthopaedica Scandinavica Supplementum No. 117. Munksgaard, Copenhagen, 1968.

World Directory of Schools of Public Health, 1965. World Health Organization, Geneva. Cloth. Pp. 232. Price, $7.00. The American Public Health Association, Inc., 1740 Broadway, New York, N. Y. 10019, 1968.

Chronic Ulcerative Colitis: A Lifelong Study. By J. Arnold Bargen, M.D., Clinical Professor of Medicine, University of California at Irvine; Consultant in Gastroenterology, Riverside Medical Clinic, Riverside, Calif.; Emeritus Professor of Medicine, Mayo Graduate School of Medicine; Former Chairman, Department of Gastroenterology, The Mayo Clinic, Rochester, Minn.; Senior Consultant in Gastroenterology, Scott and White Clinic; Director of Medical Education, Scott and White Memorial Hospital and Scott, Sherwood and Brindley Foundation, Temple Texas. Cloth. Pp. 123, with many illustrations. Price $7.50. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill. 62703, 1969.

NASA Contributions to Bioinstrumentation Systems: A Survey. By Gershon Weltman, Moshe Klagsbrun, Donald Ukkestad, and Ben Ettelson. Prepared under contract for NASA by Spacelabs, Inc. Paper. Pp. 97, with some illustrations. Price, $1.00. NASA Sp-5054. Technology Utilization Division, Office of Technology Utilization, National Aeronautics and Space Administration, Washington, D. C. For sale by the Superintendent of Documents, U. S. Government Printing Office, Washington, D. C. 20402, 1968.

Echoencephalography in Infants and Children; Comparison with Cerebral Pneumography in Measuring Ventricular Size. By Iréne Sjögren, Kjell Bergström and Herman Lodin, Department of Paediatrics and Diagnostic Radiology, University Hospital, Uppsala, Sweden. Acta Radiologica Supplementum 278. Paper. Pp. 80, with a few illustrations. Price, Sw. Kr. 35;-. Acta Radiologica, Box 2052, Stockholm 2, Sweden, 1968.

Radiation Induced Asymmetry and Lymphoma of Thymus in Mice. By Bertil Järplid, Division of Radiobiology, Research Institute of National Defence, Sundbyberg, Sweden. Acta Radiologica Supplementum 279. Paper. Pp. 98, with some illustrations. Price, Sw. Kr. 35;-. Acta Radiologica, Box 2052, Stockholm, Sweden, 1968.

SOCIETY PROCEEDINGS

MEETINGS OF RADIOLOGICAL SOCIETIES*

UNITED STATES OF AMERICA

AMERICAN ROENTGEN RAY SOCIETY
Secretary, Dr. Ted F. Leigh, Emory University Clinic, Atlanta, Ga. 30322. Annual Meeting: Washington-Hilton Hotel, Washington, D.C., September 30–October 3, 1969.

AMERICAN RADIUM SOCIETY
Secretary, Dr. John V. Blady, The Parkway House, 2201 Benjamin Franklin Parkway, Philadelphia, Pa. 19130. Annual meeting: Bellevue Stratford Hotel, Philadelphia, Pa., April, 28–30, 1969.

RADIOLOGICAL SOCIETY OF NORTH AMERICA
Secretary-Treasurer, Dr. Maurice Doyle Frazer, 1744 South Fifty-eighth St., Lincoln, Neb. Annual meeting: Palmer House, Chicago, Ill., November 30–December 5, 1969.

AMERICAN COLLEGE OF RADIOLOGY
Executive Director, William C. Stronach, 20 N. Wacker Drive, Chicago 6, Ill. Annual meeting: Statler-Hilton Hotel, Dallas, Tex., March 31–April 4, 1970.

SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION
Secretary, Dr. Kenneth L. Krabbenhoft, Harper Hospital, Detroit, Mich. 48201. Annual meeting: New York, N. Y., July 13–17, 1969.

AMERICAN BOARD OF RADIOLOGY
Secretary, Dr. C. Allen Good. Correspondence should be directed to Kahler Center Building, Rochester, Minn. 55901.
The oral examinations will be held at the Pittsburgh Hilton Hotel, Pittsburgh, Pa., June 2–6, inclusive, 1969; and at the Statler Hilton Hotel, Dallas, Texas, Dec. 8–12, inclusive, 1969.
The written examination will be held in selected sites, Saturday, June 21, 1969.
The deadline for filing applications for any of the above three examinations was December 31, 1968.

AMERICAN ASSOCIATION OF PHYSICISTS IN MEDICINE
Secretary, Leonard Stanton, Hahnemann Medical College, 230 N. Broad St., Philadelphia, Pa. 19102.

AMERICAN SOCIETY OF THERAPEUTIC RADIOLOGISTS
Secretary, Dr. J. A. del Regato, Penrose Cancer Hospital, Colorado Springs, Colo. 80907.

AMERICAN SOCIETY FOR DIAGNOSTIC ULTRASOUND
Secretary, Dr. Charles C. Grossman, 552 N. Neville St., Pittsburgh, Pa. 15213.

AMERICAN SOCIETY OF NEURORADIOLOGY
Secretary-Treasurer, Dr. Alan E. Zimmer, Danbury, Conn. 06810.

TWELFTH INTERNATIONAL CONGRESS OF RADIOLOGY
President, Dr. Kempo Tsukamoto, 9-1, 4-chome, Angewa, Chiba, Japan. Meeting: Hotel New Otani, Tokyo, Japan, Oct. 6–11, 1969.

TENTH INTER-AMERICAN CONGRESS OF RADIOLOGY
Counselor for the United States, Dr. Juan A. del Regato, Penrose Cancer Hospital, 2215 North Cascade Ave., Colorado Springs, Colo. 80907.
President, Dr. Juan A. del Regato, Colorado Springs, Colo., USA.
Secretary, Dr. F. Bloedorn, Boston, Mass., USA.
Meeting: San Juan, Puerto Rico, 1971.

INTER-AMERICAN COLLEGE OF RADIOLOGY
President, Dr. Oscar Soto, H. Urteaga 480, Lima, Perú.

ALABAMA RADIOLOGICAL SOCIETY
Secretary, Dr. Walter Brower, Birmingham, Ala. Meets time and place of Alabama State Medical Association.

ALASKA RADIOLOGICAL SOCIETY
Secretary, Dr. Bruce C. Wright, Providence Hospital, Anchorage, Alaska. Meets third Wednesday each month.

ARIZONA RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Robert E. Steyskal, 550 W. Thomas Rd., Phoenix, Ariz. 85013. Two regular meetings a year. Annual meeting at time and place of State Medical Association and interim meeting six months later.

ARKANSAS CHAPTER OF AMERICAN COLLEGE OF RADIOLOGY
Secretary-Treasurer, Dr. Wilma C. Diner, Univ. of Arkansas Medical Center, Little Rock, Ark. 72201.

ARKANSAS RADIOLOGICAL SOCIETY
Secretary, Dr. Charles W. Anderson, 1108½ Poplar, Pine Bluff, Ark. Meets every three months and also at time and place of State Medical Association.

ASSOCIATION OF UNIVERSITY RADIOLOGISTS
Secretary-Treasurer, Dr. Alexander Gottschalk, University of Chicago Medical School, Chicago, Ill. 60637. Annual Meeting: University of California, San Francisco, May 7–10, 1969.

ATLANTA RADIOLOGICAL SOCIETY
Secretary, Dr. Donald R. Rooney, Burnt Hickory Road, Marietta, Ga. Meets monthly except during three summer months, on third Tuesday, at the Academy of Medicine, Atlanta, Ga., at 8:00 P.M.

BAVARIAN-AMERICAN RADIOLOGIC SOCIETY
Advisor, Colonel Paul E. Sieber. *Secretary*, Major Peter B. Riesz, USAH Bad Cannstatt, APO 09154, New York. N. Y. Meets quarterly.

BLOCKLEY RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. R. John Gould, 41 Lombardy Rd., Drexel Hill, Pa. 19026.

BLUEGRASS RADIOLOGICAL SOCIETY
Secretary-Treasurer, Joseph A. Sayeg, Ph.D., Radiation Physicist, University of Kentucky, Lexington, Kentucky 40506. The Society meets once each month during the school year.

BROOKLYN RADIOLOGICAL SOCIETY
Secretary, Dr. Coleman H. Rosenberg, 81–10 Chevy Chase St., Jamaica, N.Y. 11432. Meets first Thursday of each month, October through June.

BUFFALO RADIOLOGICAL SOCIETY
Secretary, Dr. Courtland Van Deusen, 817 Main St., Niagara Falls N. Y. 14301. Meets second Monday evening each month, October to May inclusive., at University Club.

CALIFORNIA RADIOLOGICAL SOCIETY
Secretary-Treasurer: Dr. Leroy K. Mills, 3157 Oakcliff Circle, Carmichel, Calif. 95608. Meets annually during meeting of California Medical Association.

CATAWBA VALLEY RADIOLOGICAL SOCIETY
Secretary, Dr. Emmett R. White, P. O. Box 303, Rutherford College, N. C. 28671. Meets every Friday, Dept. of Radiology, Valdese General Hosp., Valdese, N. C., at 12:00 NOON.

CENTRAL NEW YORK RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. David N. Cheris, Community General Hospital of Greater Syracuse, Broad Road, Syracuse, N. Y. 13215. Meets first Monday each month, October through May.

CENTRAL OHIO RADIOLOGICAL SOCIETY
Secretary, Dr. Ollie E. Southard, 2787 Tudor Rd., Columbus, O. 43209. Meets second Thursday in October, November, January, and March 15 and May 19 at Fort Hayes Hotel, Columbus, Ohio.

* Secretaries of societies are requested to send timely information promptly to the Editor.

Chicago Roentgen Society
Secretary-Treasurer, Dr. Howard C. Burkhead, 2650 Ridge Ave., Evanston, Ill. 60202. Meets third Wednesday of each month, October to April, except December, at the University Club of Chicago.

Cleveland Radiological Society
Secretary-Treasurer, Dr. James Farmer, 18869 Canyon Rd. Fairview Park, Ohio 44126. Meetings at 7:00 P.M. on fourth Monday of October, November, January, February, March and April.

Colorado Radiological Society
Secretary, Dr. Charles E. Seibert, Department of Radiology, Swedish Hospital, 501 E. Hampton, Englewood, Colo. 80110. Meets third Friday of each month at Denver Athletic Club from September through May.

Connecticut Valley Radiologic Society
Secretary, Dr. William W. Walthall, Jr., 130 Maple St., Springfield, Mass. Meets in April and October.

Dallas-Fort Worth Radiological Society
Secretary-Treasurer, Dr. R. W. Perrin, P.O. Box 5999, Dallas, Texas 75222. Meets the 3rd Monday of every month at 6:30 P.M., at the Cibola Inn, Arlington, Texas.

Detroit Roentgen Ray Society
Secretary, Dr. David P. Corbett, Harper Hospital, Detroit, Mich. 48201. Meets monthly, first Thursday, October through May, at David Whitney House, 1010 Antietam, at 6:30 P.M.

East Bay Radiological Society
Secretary, Dr. Allen B. Freitag, 411 30th Str., Oakland, Calif. 94609. Meets first Thursday each month, Oct. through May, at University Club, Oakland, Calif.

East Tennessee Radiological Society
Secretary-Treasurer, Dr. Eberhard F. Besemann, Baroness Erlanger Hospital, Chattanooga, Tenn. 37403. Meets in January and September.

Florida Radiological Society
Secretary, Dr. Robert H. Nickau, Good Samaritan Hospital, West Palm Beach, Fla. 33402. Meets twice annually, in the spring with the annual State Society Meeting and in the fall.

Florida West Coast Radiological Society
Secretary-Treasurer, Dr. Allen L. Sheer, University Community Hospital, 13505 N. 31st St., Tampa, Fla. 33612. Meets in January, March, May, July, September and November.

Georgia Radiological Society
Chapter of the American College of Radiology
Secretary, Dr. Walker Harris, The Medical Center, Columbus, Georgia 31902. Meets in spring and fall at Annual State Society Meeting.

Greater Cincinnati Radiological Society
Secretary-Treasurer, Dr. Owen L. Brown, 2421 Auburn Ave., Cincinnati, Ohio 45219.

Greater Louisville Radiological Society
Secretary-Treasurer, Dr. L. D. LeNeave, 315 E. Broadway, Louisville, Ky. 40202. Meets monthly.

Greater Miami Radiological Society
Secretary-Treasurer, Dr. Sylvan H. Sarasohn, P. O. Box 1256, North Miami, Fla. 33161. Meets monthly, third Wednesday at 8:00 P.M. at Jackson Memorial Hospital, Miami, Fla.

Greater St. Louis Society of Radiologists
Secretary-Treasurer, Dr. Roland P. Ernst, 3720 Washington Ave., St. Louis, Mo. 63108.

Hawaii Radiological Society
Secretary-Treasurer, Dr. Thomas C. Brown, 1697 Ala Moana Blvd., Honolulu, Hawaii 96815. Meets third Monday of each month at 7:30 P.M.

Health Physics Society
Secretary, R. J. Augustine, National Center for Radiologic Health, 1901 Chapman Ave., Rockville Md. 20852.

Houston Radiological Society
Secretary, Dr. Eleanor Montague, 6516 Bertner, Houston, Tex. 77025. Meets fourth Monday of each month, except June, July, August and December, at 6:00 P.M., at 103 Jesse H. Jones Library Building, Texas Medical Center, Houston, Tex. 77025.

Idaho State Radiological Society
Secretary, Dr. George H. Harris, Bannock Memorial Hospital, Pocatello, Idaho. Meets in the spring and fall.

Illinois Radiological Society, Inc.
Secretary, Dr. C. R. Markivee, 674 North Seminary St., Galesburg, Ill. 61401. Meets in the spring and fall.

Indiana Roentgen Society, Inc.
Secretary, Dr. Edwin F. Koch, Jr., 915 University Ave., Muncie, Ind. 47303. Meets first Sunday in May and during fall meeting of Indiana State Medical Association.

Iowa Radiological Society
Secretary-Treasurer, Dr. J. H. Lohnes, 1948 First Ave., N.E., Cedar Rapids, Iowa 52402. Luncheon and business meeting during annual session of Iowa State Medical Society. The scientific section is held in the autumn.

Kansas Radiological Society
Secretary-Treasurer, Dr. Robert C. Lawson, 310 Medical Arts Bldg., 10th and Horne, Topeka, Kan. Meets in spring with State Medical Society and in winter on call.

Kentucky Chapter, American College of Radiology
Secretary-Treasurer, Dr. Ralph C. Quillin, 1221 S. Broadway, Lexington, Ky. 40504. Meets in April and September.

Kings County Radiological Society
Secretary, Dr. Sidney Hendler, 1880 Ocean Ave., Brooklyn 30, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

Knoxville Radiological Society
Secretary, Dr. Clifford L. Walton, Blount Professional Bldg., Knoxville 20, Tenn. Meetings are held the third Monday of every other month at the University of Tennessee Memorial Research Center and Hospital.

Long Island Radiological Society
Secretary, Dr. Robert J. Hochstim, 1200 Stewart Ave., Garden City, N. Y. 11533. Meets monthly.

Los Angeles Radiological Society
Secretary, Dr. John L. Gwinn, Childrens Hospital of Los Angeles, 4650 Sunset Blvd., Los Angeles, Calif. 90027. Meets second Wednesday of month in September, November, January, April and June at Los Angeles County Medical Association Building, Los Angeles, Calif.

Louisiana-Texas Gulf Coast Radiological Society
Secretary-Treasurer, Dr. Edward A. Sheldon, 109 Doctors Bldg., Beaumont, Texas 77701.

Maine Radiological Society
Secretary-Treasurer, Dr. Robert A. Bearor, Maine Medical Center, Portland, Maine 04102. Meets in June, September, December and April.

Maryland Radiological Society
Secretary, Dr. Henry Startzman, Medical Arts Building, Baltimore, Md.

Massachusetts Radiological Society
Secretary, Dr. Jerome H. Shapiro, Department of Radiology, Boston City Hospital, 818 Harrison Ave., Boston, Mass. 02118.

Memphis Roentgen Society
Secretary-Treasurer, Dr. Webster Riggs, Jr., The University of Tennessee College of Medicine, Department of Radiology, Walter F. Chandler Bldg., 865 Jefferson Ave., Memphis, Tenn. 38103. Meets first Monday of each month at John Gaston Hospital.

Miami Valley Radiological Society
Secretary, Dr. Darwood B. Hance, Reid Memorial Hospital, Richmond, Indiana. Meets third Thursday of fall, winter and spring months at 7:30 P.M. at Miami Valley Hospital, Dayton, Ohio.

Mid-Hudson Radiological Society
Secretary-Treasurer, Dr. Herbert S. Berlin, Hopewell Junction, N. Y. Meets 7:00 P.M., first Wednesday of each month, September to May.

Milwaukee Roentgen Ray Society
Secretary-Treasurer, Dr. James E. Bell, 8700 W. Wiscon-

sin Ave., Milwaukee, Wis. 53213. Meets monthly on fourth Monday, October through May, at University Club.

Minnesota Radiological Society
Secretary-Treasurer, Dr. Warren L. Kump, 4243 Glenwood Ave., Minneapolis, Minn. 55422. Meets twice annually, fall and winter.

Mississippi Radiological Society
Secretary-Treasurer, Dr. Dan T. Keel, Jr., 504 Chippewa St., Brookhaven, Miss. Meets third Thursday of each month at the Heidelberg Hotel, Jackson, at 6:00 P.M.

Missouri Radiological Society
Secretary-Treasurer, Dr. Arthur A. Porporis, 100 N. Euclid Ave., St. Louis, Mo. 63108.

Montana Radiological Society
Secretary, Dr. Colvin H. Agnew, Doctors' Building, 1231 N. 29th Street, Billings, Montana 59101. Meets in Glacier National Park, July 23–25, 1969.

Nebraska State Radiological Society
Secretary-Treasurer, Dr. Otto A. Troester, 924 Sharp Building, Lincoln, Nebraska 60508. Meets third Wednesday of each month at 6 P.M. in Omaha or Lincoln.

Nevada Radiological Society
Secretary, Dr. William G. Arbonies, Department of Radiology, St. Mary's Hospital, Reno, Nev.

New England Roentgen Ray Society
Secretary, Dr. Morris Simon, 330 Brookline Ave., Boston, Mass. 02115. Meets third Friday of each month, October through May, at The Longwood Towers, 20 Chapel Street, Brookline, Mass., at 4:30 P.M. The Annual Meeting will be held May 24 and 25, 1969, at the Hotel Belmont, West Harwich by-the-sea, Cape Cod, Mass. The guest speaker, Dr. Lucy Frank Squire, will present the Twenty-fifth George W. Holmes Lecture.

New Hampshire Roentgen Ray Society
Secretary, Dr. Paul Y. Hasserjian, 1470 Elm St., Manchester, N. H. Meets four to six times yearly.

New Mexico Association of Radiologists
Secretary-Treasurer, Dr. Justin J. Wolfson, Department of Radiology, Bernalillo County-Indian Hospital, Albuquerque, New Mexico.

New Mexico Society of Radiologists
Secretary, Dr. Phil Fox, Albuquerque, New Mexico. Four meetings annually, three held in Albuquerque, N. M., and one held at time and place of New Mexico State Medical Society annual meeting.

New York Roentgen Society
Secretary-Treasurer, Dr. Samuel H. Madell, 1 E. 82nd St New York, N. Y. 10024. Meets monthly on third Monday at the New York Academy of Medicine at 4:30 P.M. Spring Conference: Waldorf Astoria Hotel, April 24–26, 1969.

New York State Chapter of the American College of Radiology, Inc.
Secretary-Treasurer, Dr. John W. Colgan, 273 Hollywood Ave., Rochester, N. Y., 14618.

North Carolina Chapter of ACR.
Secretary-Treasurer, Dr. Ira Bell, Hickory, N. C.

North Carolina Radiological Society
Secretary, Dr. E. H. Schultz, North Carolina Memorial Hospital, Chapel Hill, N. C. Meets in the spring and fall each year.

North Dakota Radiological Society
Secretary, Dr. A. Ohrt, 408 Medical Arts Bldg., Fargo, N. D. 58102. Meets at time of State Medical Association meeting. Other meetings arranged on call of the President.

North Florida Radiological Society
Secretary, Dr. Charles H. Newell, 800 Miami Road, Jacksonville 7, Fla. Meets quarterly in March, June, September and December.

Northeastern New York Radiological Society
Secretary, Dr. Herbert F. Reilly, Jr., 12 Sandalwood Rd., Scotia, New York 12302. Meets in Albany area on third Wednesday of October, November, March, April, and May.

Northern California Radiological Society
Secretary-Treasurer, Ivan D. Siddons, 3701 J. St., Suite 106, Sacramento, Calif. 95816. Meets fourth Monday of Sept., Nov., Jan., March and May at the Sutter Club in Sacramento.

Northwestern Ohio Radiological Society
Secretary, Dr. Vito J. Zupa, Mercy Hospital, Department of Radiology, Toledo, Ohio.

Ohio State Radiological Society
Secretary, Dr. Robert D. Berkebile, Elyria Memorial Hospital, Elyria, Ohio 44035.

Oklahoma State Radiological Society
Secretary, Dr. Donald F. Mauritson, 100 Utica Square Med. Center, Tulsa, Okla. 74114. Meets in January, May and October.

Orange County Radiological Society
Secretary, Dr. Richard Simpson, Hoag Memorial Hospital, 301 Newport Ave., Newport Beach, California. Meets on fourth Tuesday of the month, excluding June, July, August, and December, at the Orange County Medical Association Bldg., Orange, Calif.

Oregon Radiological Society
Secretary-Treasurer, Dr. Clinton B. Sayler, 214 Medical Dental Bldg., Portland, Oregon 97205. Meets on second Wednesday of month, October through April, at the University Club, Portland, Ore.

Orleans Parish Radiological Society
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans, La. 70113. Meets second Tuesday of each month.

Pacific Northwest Radiological Society
Secretary-Treasurer, Dr. Marvin Wallace, 555 108th Ave. N. E., Bellevue, Washington 98004.

Pennsylvania Radiological Society
Secretary, Dr. Theodore A. Tristan, Harrisburg, Polyclinic Hosp., Harrisburg, Pa. 17105.

Philadelphia Roentgen Ray Society
Secretary, Dr. C. Jules Rominger, Misericordia Hospital, 54th St. and Cedar Ave., Philadelphia, Pa. 19143. Meets first Thursday of each month at 5 P.M., from October to May in Thompson Hall, College of Physicians.

Pittsburgh Roentgen Society
Secretary, Dr. Edward R. Seitz, 601 Jenkins Bldg., Pittsburgh, Pa. 15222. Meets second Wednesday of month, October through June, at Park Schenley Restaurant.

Radiation Research Society
Secretary-Treasurer, Dr. Gail D. Adams, Dept. of Radiology, Univ. of Oklahoma Medical Center, Oklahoma City, Oklahoma 73104. Annual Meeting: Netherland Hilton Hotel, Cincinnati, Ohio, May 18–22, 1969.

Radiological Society of Connecticut, Inc.
Secretary-Treasurer. Dr. Henry J. Fox, 10 Washington Ave., Bridgeport, Conn. Meetings are held quarterly.

Radiological Society of Greater Cincinnati
Secretary-Treasurer, Dr. Donald E. Gunderson, 3553 Bayard Dr., Cincinnati, Ohio 45208. Meets first Monday of each month at Cincinnati Academy of Medicine.

Radiological Society of Greater Kansas City
Secretary, Dr. J. Stewart Whitmore, 1010 Rialto Bldg., Kansas City, Mo. Meets last Friday of each month.

Radiological Society of Kansas City
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

Radiological Society of Louisiana
Secretary, Dr. Lester W. Eavenson, 2700 Napoleon Ave., New Orleans 15, La. Meets semiannually, during Louisiana State Medical Society meeting and 6 months later.

Radiological Society of New Jersey
Secretary, Dr. John W. Marquis, 12 Hawthorne Ave., East Orange, N. J. 07018. Meets in Atlantic City at time of State Medical Society meeting and in October or November in Newark, N. J.

Radiological Society of Rhode Island
Secretary-Treasurer, Dr. John M. Vesey, 1196 Elmwood Ave., Cranston, R. I.

Radiological Society of South Dakota
Secretary-Treasurer, Dr. Donald J. Peik, 303 S. Minnesota Ave., Sioux Falls, S. D.

Radiological Society of Southern California
Secretary-Treasurer, Dr. Robert G. Williams, The Santa Barbara Medical Clinic, P.O. Box 1200, Santa Barbara, Calif. 93102. Meets three times a year, usually October, February and May.

Radiological Society of the State of New York
Secretary-Treasurer, Dr. John W. Colgan, 273 Hollywood Ave., Rochester, N. Y. 14618.

Redwood Empire Radiological Society
Secretary, Dr. Lee F. Titus, 164 W. Napa St., Sonoma, Calif. Meets second Monday every other month.

Richmond County Radiological Society
Secretary, Dr. W. F. Hamilton, Jr., University Hospital, Augusta, Ga. Meets first Thursday of each month at various hospitals.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. Kenneth E. Robinson, Rochester General Hospital, 1425 Portland Ave., Rochester, N. Y. 14621. Quarterly meetings on the call of the President, at the Rochester Academy of Medicine.

Rocky Mountain Radiological Society
Secretary-Treasurer, Dr. Robert W. Lackey, 4200 E. Ninth Ave., Denver, Colo. 80220. Annual meeting: Brown Palace Hotel, Denver, Colo., Aug. 21–23, 1969.

San Antonio-Military Radiological Society
Secretary, Dr. Hugho F. Elmendorf, Jr., 730 Medical Arts Bldg., San Antonio 5, Tex. Meets third Wednesday of each month in Fort Sam Houston Officer's Club at 6:30 P.M.

San Diego Radiological Society
President-Secretary, Charles R. Henkelmann, 3909 Palm Drive, Bonita, Calif. 92002. Meets first Wednesday of each month at the Town & Country Motel.

San Francisco Radiological Society
Secretary-Treasurer, Dr. Warren M. Russell, Franklin Hospital, Castro & Duboce, San Francisco, Calif. 94114. Meets quarterly at various hospitals (contact Secretary).

Santa Clara County Radiological Society
Secretary, Dr. John J. Berg, 45 So. 17th Street, San Jose, Calif. 95112. Meets monthly at the Santa Clara County Medical Association Bldg., 700 Empey Way, San Jose, Calif.

Section on Radiology, California Medical Association
Secretary, Dr. William H. Graham, 630 East Santa Clara St., San Jose, Calif.

Section on Radiology, Medical Society of the District of Columbia
Secretary-Treasurer, Dr. Louis Wener, Cafritz Memorial Hosp., 1310 Southern Ave., S.E., Washington, D. C. 20032. Meets at Medical Society Library, third Wednesday of January, March, May and October at 8:00 P.M.

Section on Radiology, Southern Medical Association
Secretary, Dr. Phillip W. Voltz, Jr., 120 Medical Professional Bldg., San Antonio, Texas 78212. Annual meeting: To be announced.

Section on Radiology, Texas Medical Association
Secretary, Dr. George F. Crawford, St. Elizabeth Hospital, Beaumont, Tex. Meets annually with the Texas Medical Association.

Shreveport Radiological Club
Secretary, Dr. W. R. Harwell, 608 Travis St., Shreveport, La. Meets monthly on third Wednesday at 7:30 P.M., September to May inclusive.

Society for Pediatric Radiology
Secretary, Dr. John L. Gwinn, Children's Hospital, 4614 Sunset Blvd., Los Angeles 27, Calif. Annual meeting: Washington-Hilton Hotel, Washington, D.C., September 29, 1969.

Society of Nuclear Medicine
Secretary, Mr. C. Craig Harris, Oak Ridge National Laboratories, Oak Ridge, Tenn. *Administrator*, Mr. Samuel N. Turiel, 430 N. Michigan Ave., Chicago 11, Ill. Annual meeting: Jung Hotel, New Orleans La., June 22–28, 1969.

South Bay Radiological Society
Secretary, Dr. Emerson C. Curtis, University Dr., Menlo Park, Calif. 94025. Meets second Wednesday of each month.

South Carolina Radiological Society
Secretary, Dr. George W. Brunson, 1406 Gregg St., Columbia, S. C. Annual meeting (primarily business) in conjunction with the South Carolina Medical Association meeting in May. Annual fall scientific meeting at time and place designated by the president.

South Dakota Radiological Society
Secretary, Dr. Donald J. Peik, 1417 S. Minnesota Ave., Sioux Falls, S. Dak. Meets in spring with State Medical Society and in fall.

Southern California Radiation Therapy Society
Secretary-Treasurer, Dr. Aaron G. Fingerhut, 1000 W. Carson St., Torrance, Calif. 90502. Meets quarterly.

Southern Radiological Conference
Secretary-Treasurer, Dr. Marshall Eskridge, Mobile Infirmary, P.O. Box 4097, Mobile, Ala. 36604. Annual meeting: Grand Hotel, Pointe Clear, Ala. 36564, Jan. 30–Feb. 1, 1970.

Southwestern Radiological Society
Secretary, John M. McGuire, 904 Chelsea, El Paso, Tex. Meets last Monday of each month at 6:30 P.M. in the Paso del Norte Hotel.

Tennessee Radiological Society
Secretary-Treasurer, Dr. Marion E. Spurgeon, Memorial Hosp., Clarksville, Tenn. 37040. Meets annually at the time and place of the Tennessee State Medical Association meeting.

Texas Radiological Society
Secretary, Dr. Herman C. Sehested, 815 Medical Arts Bldg., Fort Worth 2, Tex. Annual meeting to be announced.

Tri-State Radiological Society
Secretary, Dr. John H. Marchand, Jr., Methodist Hospital, Henderson, Ky. Meets third Wednesday of Oct., Jan., March and May, 8:00 P.M., Elks Club in Evansville, Ind.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7:00 P.M. at University Hospital, Ann Arbor Mich.

Upper Peninsula Radiological Society
Secretary, Dr. A. Gonty, Menominee, Mich. Meets quarterly.

Utah State Radiological Society
Secretary-Treasurer, Dr. Leon M. Neal, St. Benedict's Hospital, 3000 Polk Ave., Ogden, Utah 84403. Meets fourth Wednesday in January, March, May, September and November at Holy Cross Hospital.

Vermont Radiological Society
Secretary, Dr. John R. Williams, 160 Allen St., Rutland, Vt.

Virginia Radiological Society
Secretary-Treasurer, Dr. K. Kenneth Wallace, Jr., Virginia Beach, Va.

Washington State Radiological Society
Secretary-Treasurer, Dr. Paul S. Paulson, 1001 Broadway, Seattle, Washington 98122. Meets quarterly.

West Virginia Radiological Society
Secretary-Treasurer, Dr. George G. Green, Department of Radiology, W. Va. Univ. Medical Center, Morgantown, W. Va. 26506. Meets concurrently with Annual Meeting of West Virginia State Medical Society; other meetings arranged by program committee.

Westchester County Radiological Society
Secretary, Dr. Arnold Gerson, Medical Arts Bldg., Mt.

Vernon, N. Y. Meets on third Tuesday of January and October and on two other dates.

Wisconsin Radiological Society
Secretary-Treasurer, Dr. Robert E. Douglas, 117 N. Commercial St., Neenah, Wis. 54956. Meets twice a year, May and September.

Wyoming Radiological Society
Secretary, Dr. J. D. Grant, Memorial Hosp., Sheridan, Wyo. Meets in fall with State Medical Society and in spring on call of President.

Mexico, Puerto Rico and Central America

Asociación Costariccense de Radiología
Secretary, Dr. Jorge Vargas Segura, Apartado 5367, San José, Costa Rica.

Asociación de Radiólogos de Centro America y Panamá. Comprising: Guatemala, El Salvador, Honduras, Nicaragua, Costa Rica and Panamá.
Secretary-General, Dr. Roberto Calderón, Calle Central Oeste No. 218, Managua, Nicaragua, Central America. Meets annually in a rotating manner in the six countries.

Sociedad de Radiología de El Salvador
Secretary, Dr. Julio Astacio, 5a Av. Nte. No. 434, San Salvador, Rep. El Salvador.

Sociedad de Radiología de Guatemala
Secretary, Dr. Carlos E. Escobar, 9ª. Calle A 0-05, Zona 1, Guatemala.

Sociedad Mexicana de Radiología, A.C.
Coahuila No. 35, México 7, D. F.
Secretary-General, Dr. Ramón Ruenes.
Meets first Monday of each month.

Asociación Puertorriqueña de Radiología
Secretary, Dr. R. B. Díaz Bonnet, Suite 504, Professional Bldg., Santurce, Puerto Rico.

Sociedad Radiológica Panameña
Secretary, Dr. L. Arrieta Sánchez, Apartado No. 6323, Panamá, R. de P. Meets monthly in a department of radiology of a local hospital chosen at preceding meeting.

Sociedad Radiológica de Puerto Rico
Secretary, Dr. Felipe N. de Jesús, Apt. 9387, Santurce, Puerto Rico. Meets second Thursday of each month at 8:00 P.M. at the Puerto Rico Medical Association Bldg. in San Juan.

British Commonwealth of Nations

Association of Radiologists of the Province of Quebec
Secretary, Dr. R. Robillard, Notre-Dame Hospital, 1560 Sherbrooke St., East, Montreal, Que., Canada. Meets four times a year.

British Institute of Radiology
Honorary Secretary, Dr. G. H. du Boulay, 32 Welbeck St., London, W. 1, England. Meets monthly from October until May.

Canadian Association of Physicists, Division of Medical and Biological Physics.
Honorary Secretary-Treasurer, Paul M. Pfalzner, Department of Therapeutic Radiology, University of Western Ontario, London, Ontario, Canada.

Edmonton and District Radiological Society
Secretary, J. D. R. Miller, M.B., University of Alberta Hospital, Edmonton, Alberta, Canada. Meets third Thursday of each month October to May, except December, at various Edmonton Hospitals.

Faculty of Radiologists
Honorary Secretary, Dr. J. N. Pattinson, 47 Lincoln's Inn Fields, London, W.C.2, England.

Faculty of Radiologists, Royal College of Surgeons in Ireland
Registrar, Dr. H. O'Flanagan, F.R.C.P.I., D.P.H., 123 St. Stephens Green, Dublin 2, Ireland.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets third Friday each month at 4:45 P.M. at the Royal Society of Medicine, 1 Wimpole St., London, W. 1, England.

Canadian Association of Radiologists
Honorary Secretary-Treasurer, Dr. Maurice Dufresne, *Associate Honorary Secretary-Treasurer*, Dr. F. Robert MacDonald, 1555 Summerhill Ave., Montreal 25, Que., Canada. Annual Meeting: To be announced.

Montreal Radiological Study Club
Secretary, Dr. Leonard Rosenthall, Montreal General Hospital, Montreal, Que., Canada. Meets first Tuesday evening, October to April.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Société Canadienne-Française de Radiologie
Secretary General, Dr. Guy Duckett, 1385 est, rue Jean Talon, Montréal P.Q., Canada. Meets every third Tuesday from October to April. Annual Meeting: Nov. 13–15, 1969.

Toronto Radiological Society
Secretary, Dr. George Wortzman, Toronto General Hosp., Toronto 12, Ont., Canada. Meets second Monday of each month, September through May.

College of Radiologists of Australasia
Honorary Secretary, Dr. T. P. Loneragan, c/o British Medical Agency, 135 Macquarie St., Sydney, N.S.W., Australia.

South America

Asociación Argentina de Radiología
Secretary, Dr. Lidio G. Mosca, Avda. Gral. Paz 151, Córdoba, Argentina. Meetings held monthly.

Ateneo de Radiologia
Secretary, Dr. Victor A. Añaños, Instituto de Radiologia, Santa Fe 3100, Rosario, Argentina. Meets monthly on second and fourth Fridays at 7:00 P.M. in the Hospital Nacional de Centenario, Santa Fe 1300, Rosario.

Colégio Brasileiro de Radiologia
Secretary-General, Dr. Miguel Mario Céntola, Caixa Postal 5984, São Paulo, Brazil.

Sociedad Argentina de Radiologia
Secretary-General, Dr. Oswaldo E. Zerbo, Santa Fe 1171, Buenos Aires. Meetings are held monthly.

Sociedad Boliviana de Radiología
Secretary, Dr. Javier Prada Méndez. Casilla 1182, La Paz, Bolivia. Meets monthly. General assembly once every two years.

Sociedade Brasileira de Radiologia
Secretary, Dr. Armando Rocha Amoédo, Cxa Postal 1532, Rio de Janeiro, Brazil. General Assembly meets every two years in December.

Sociedade Brasileira de Radioterapia
Secretary, Dr. Oscar Rocha von Pfuhl, Av. Brigadeiro Luiz Antonio, 644, São Paulo, Brazil. Meets monthly on second Wednesday at 9:00 P.M. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

Sociedad Chilena de Radiología
Secretary, Dr. Manuel Concha, Casilla 13426, Santiago, Chile. Meets fourth Friday of each month.

Sociedad Colombiana de Radiologia
Secretary-General, Dr. Armando Uribe, Hospital Militar Central, Apartado aéreo No. 5804, Bogotá, Colombia. Meets last Thursday of each month.

Sociedad Ecuatoriana de Radiología y Fisioterapía
Secretary, Dr. Carlos Palau, Av. Bogotá 206, Guayaquil, Ecuador.

Sociedad Paraguaya de Radiología
Secretary, Dr. Miguel González Addone, 15 de Agosto 322, Asunción, Paraguay.

Sociedad Peruana de Radiologia
Secretary-General, Dra. Ladis Delpino, Instituto de Radiología "Cayetano Heredia" Hospital Arzobispo Loayza, Lima, Perú. Meets monthly except during January, February and March.

Sociedad de Radiologica del Atlantico
Secretary, Dr. Raul Fernandez, Calle 40 #41–110, Baranquilla, Colombia. Society meets monthly at the Instituto de Radiología.

Sociedad de Radiología, Cancerología y Física Médica del Uruguay
Secretary-General, Dr. José Claussius, Av. Agraciada 1464, piso 13, Montevideo, Uruguay.

Sociedade de Radiología de Pernambuco
Secretary, Dr. Manoel Medeiros, Instituto de Radiologia da Faculdade de Medicina da Universidade do Recife, Caixa Postal 505, Pernambuco, Brazil.

Sociedad de Roentgenología y Medicina Nuclear de la Provincia de Córdoba
Secretary-General, Dr. Lucas C. Di Rienzo, Ave. Grl. Paz. 151, Córdoba, Argentina.

Sociedad Venezolana de Radiología
Secretary-General, Dr. Modesto Rivero Gonzáles, Apartado No. 9362 Candelaria, Caracas, Venezuela. Meets monthly, third Friday at Colegio Médico del Distrito Federal, Caracas.

Continental Europe

Österreichische Röntgen-Gesellschaft
President, Dr. Konrad Weiss, Mariannengasse 10, Vienna 9, Austria. Meets second Tuesday of each month in Allgemeine Poliklinik.

Société Royale Belge de Radiologie
General Secretary, Prof. Simon Masy, Louvain, Belgium. Meets in February, March, May, June, September, October, November and December.

Société Européenne de Radiologie Pédiatrique
Permanent Secretary, Dr. Jaques Sauvegrain, Hôpital des Enfants-Malades, 149, rue de Sèvres, Paris 15e, France.
General Secretary, Dr. H. Ludin, Department of Roentgenology, Basler Kinderspital, Basel, Switzerland. Annual meeting: Warsaw, Poland, May 22–24, 1969.
Secretary, Dr. Kasawery Rowinski, Zaklad Radiologii Pediatrycynej Akademii Medycznej, Marzalkowska 24, Warszawa, Poland.

Société Française d'Electroradiologie Médicale, and its branches: Société du Sud-Ouest, du Littoral Méditerranéen, du Centre et du Lyonnais, du Nord, de l'Ouest, de l'Est, et d'Alger et d'Afrique du Nord. Central Society meets third Monday of each month, except during July, August and September, rue de Seine 12, Paris, France.
Secretary-General, Dr. Ch. Proux, 9 rue Daru Paris 8e, France.

Československá Společnost pro Roentgenologii a Radiologii
Secretary, Dr. Robert Poch, Praha 12, Srobárova 50, Czechoslovakia. Meets monthly except during July, August and September. Annual general meeting.

Deutsche Röntgengesellschaft
President, Professor Dr. med. Hanno Poppe, Radiologische Univ.-Klinik, Gossler Str. 10, 34 Göttingen, Germany.

Società Italiana di Radiologia Medica e di Medicina Nucleare
Secretary, Dr. Ettore Conte, Ospedale Mauriziano Torino, Italy. Meets annually.

Nederlandse Vereniging voor Radiologie
Secretary, Dr. C. B. A. J. Puijlaert, Prof. Dondersstraat 73, Tilburg, Netherlands.

Scandinavian Radiological Society
Secretary-General, Professor C. E. Unnérus, M.D., Hagalung-Tapiola, Havsvindsvägen 5 C., Finland. Next meeting: Finland, Helsinki, June 11–14, 1969. This is the Fiftieth Anniversary Congress of the members of the 5 Scandinavian Radiological Societies, held in scandinavian languages.

Sociedad Española de Radiología y Electrología Médicas y de Medicina Nuclear
Secretary, Juan Gómez López, Villanueva, 11, Madrid 1. Meets every second Friday of each month, Oct. to June, inclusive, in Madrid.

Schweizerische Gesellschaft für Radiologie und Nuklearmedizin (Société Suisse de Radiologie et de Médecine Nucléaire)
Secretary, Dr. Max Hopf, Effingerstrasse 47, Bern, Switzerland.

Asia

Indian Radiological Association
Secretary, Dr. R. F. Sethna, Navsari Building, Hornby Road, Bombay 1, India.

Indonesian Radiological Society
Secretary, Professor Sjahriar Rasad, Taman Tjut Mutiah I Djakarta, Indonesia

Iranian Radiological Society
Secretary, Dr. Issa Yaghmai, P.O. Box No. 14-1151, Teheran, Iran. The Society meets on the second Saturday of each month.

Vol. 105, No. 4

ABSTRACTS OF RADIOLOGICAL LITERATURE

INDEX TO ABSTRACTS

ROENTGEN DIAGNOSIS

Blood and Lymph System

Hynes, D. M., and Grainger, R. G.: The angiographic demonstration of coarctation of aorta and similar anomalies 932

Head

Lewin, W.: Preliminary observations of external hydrocephalus after severe head injury 932

Neck and Chest

Hers, J. F. P.: Clinical aspects of infection with Mycoplasma pneumoniae 933

Surprenant, E. *et al.*: Changes in regional pulmonary function following bronchography 933

Cooley, D. A., and Hallman, G. L.: Surgical treatment of left ventricular aneurysm: experience with excision of postinfarction lesions in 80 patients 933

Abdomen

Burhenne, H. J.: The iatrogenic afferent-loop syndrome 934

Goulston, K., and Cooke, A. R.: Alcohol, aspirin, and gastrointestinal bleeding 934

Hamilton, J. R.: Seat-belt injuries 934

Genitourinary System

Cruess, R. L. *et al.*: Aseptic necrosis following renal transplantation 935

Klotz, P. G.: Ureteral reflux in adults 935

Hassim, A. M., Carruthers, R. H., and Lucas, C.: Bilharzial contracted bladder treated by ileocystoplasty 935

Whitaker, J., and Johnston, G. S.: Correlation of urethral resistance and shape in girls 936

RADIATION THERAPY

Davidson, J. W., and Renouf, J. H. P.: Radiographic findings in "Burkitt type" lymphoma 936

CHEMOTHERAPY

Cohn, I., Jr., Slack, N. H., and Fisher, B.: Complications and toxic manifestations of surgical adjuvant chemotherapy for breast cancer 937

ROENTGEN DIAGNOSIS

Blood and Lymph System

Hynes, David M., and Grainger, Ronald G. The angiographic demonstration of coarctation of aorta and similar anomalies. *Clin. Radiol.*, Oct., 1968, *19*, 438–456. (From: The Department of Radiology, Northern General Hospital, Sheffield 5, England.)

The authors report 78 patients with coarctation of the aorta and similar anomalies. They have a high percentage of complicated cases due primarily to the fact that all cases were not studied and only those cases of aortic coarctation with unusual anatomic or hemodynamic features were examined. The usual method of aortography involves a right axillary approach. From this way, injections can be made from the left ventricle from above the valves and from the arch itself as well as just above the coarctation. The study from the left ventricle is necessary because of the high incidence of aortic valvular disease. The approach distally from the femoral artery or a combined approach may be used in certain cases. In infants, a right-sided study is usually employed to identify other associated abnormalities. Cardioconray is the contrast medium used in this study. Anteroposterior and lateral angiograms are usually obtained. Occasionally, however, a 45° left anterior oblique view which is the optimum projection will be necessary. The authors make use of subtraction and make liberal use of pressure recording throughout the examination.

The 78 patients were divided into 6 groups.

Group I. This group contained patients with the conventional coarctation. This is composed of 3 types: (a) the short segment coarctation distal to the left subclavian artery; (b) the long segment coarctation; and (c) the coarctation complicated by aneurysm.

(a) Short segment coarctations were found in 29 patients and were composed of 4 types. These 4 types were determined depending on the length of the distal part of the aortic arch and whether the prestenotic region was wide or narrow or, as in type 4, completely atretic. Two interesting cases are reported with this segment. One contained an aberrant subclavian artery distal to the coarctation associated with unilateral rib notching on the left. This patient also had a bicuspid valve. The second case revealed an aneurysm of the right subclavian artery with an apparent complete obstruction of the aortic arch at the origin of the left common carotid artery. This proved to be erroneous at thoracotomy, but it was found that there was a "string stricture" well below a normal left subclavian artery. The angiographic misinterpretation occurred as a result of a common arterial trunk which arose from the proximal portion of the transverse arch and, since this common trunk happened to be the region of injection, it was considered to be the aortic arch, which it indeed was not.

(b) Six patients had the so-called long segment coarctations. These all occurred in young patients and required prosthesis replacement.

(c) The third type consisted of coarctations complicated by aneurysms, which were present in 5 patients. Two had aneurysms of a patent ductus associated with long segment aortic arch hypoplasia.

Group II. In this group were coarctations associated with other types of congenital heart disease. This group contained the second largest number of cases. There were 21 patients ranging in age from 1 week to 24 years. Nearly all were studied by right heart catheterization and angiography. The most frequent anomaly was a patent ductus arteriosus with both right to left and left to right shunts being demonstrated in 13 patients. Ventricular septal defect was demonstrated in 14 patients. In no patient, however, was there any evidence of an obstructive right heart lesion.

Group III. This group consisted of long segment aortic arch hypoplasia and contained 6 patients, 5 of whom were under 4 months of age. All were studied by right heart angiography and all had large intracardiac shunts. Five of the 6 patients had a single ventricle, severe aortic arch hyperplasia, and a patent ductus with a right to left shunt.

Group IV. This group consisted of the so-called aortic kink or pseudocoarctation. Each patient had no obstruction but did have a systolic murmur with an aortic outline suggestive of coarctation but no rib notching. There were 4 patients in this group. It should be stated that kinking can certainly occur in the presence of coarctation and that this should be kept in mind when a kinked aorta is suspected.

Group V. This group consisted of 3 cases of abdominal coarctation. These patients had interesting plain film roentgenographic examinations in that calcifications at the aortic narrowing were evident in all 3. In addition, the celiac artery origin was narrowed in all 3 patients and the origin of the artery occurred in the most markedly involved section of the aorta. In all 3 patients the underlying histopathology appeared to be atherosclerotic and, therefore, it is felt that this lesion may not be congenital, but acquired and may have some relation to Takayashu's syndrome.

Group VI. This group involved those patients with supravalvular aortic stenosis and typical facies associated with this lesion, which are thick everted lips, depressed nasal bridge, eyes sloping upward and inwards and mental deficiency. Severe infantile hypercalcemia is part of this syndrome. Other large artery stenosis can also accompany this syndrome, particularly involving the pulmonary and renal arteries.—*Major James Stevenson, MC*

Head

Lewin, W. Preliminary observations of exter-

nal hydrocephalus after severe head injury. *Brit. J. Surg.*, Oct., 1968, *55*, 747–751. (From: The Department of Neurological Surgery and Neurology, Addenbrooke's Hospital, Cambridge, England.)

This communication is concerned mainly with the role of obstruction in the cerebrospinal pathways after head injury and the role this may play in generalized ventricular dilatation.

A series of 59 cases of generalized ventricular dilatation after severe head injury, of which 20 showed obstructive external hydrocephalus, are discussed. Their investigation by air encephalography and isotope cisternography is described. Of the 20, 8 had symptoms and signs of raised intracranial pressure; in the other 12 the pressure was normal.

The progressive ventricular dilatation that may take place in patients with normal cerebrospinal pressure is postulated by the fact that there is a reciprocal relationship between ventricular pressure and the surface on which it acts. Thus the findings of a normal cerebrospinal pressure do not mean that progressive hydrocephalus is not taking place.

It is suggested that there may be 3 clinical syndromes after head injury, where practical possibilities of relieving a demonstrable obstructive hydrocephalus by a by-pass operation (ventriculo-atrial or ventriculoperitoneal shunt) should be considered: (1) progressive mental and physical deterioration after the acute stage is passed; (2) with symptoms and signs of raised intracranial pressure; and (3) with prolonged unconsciousness, where intracranial pressure is normal.

The initial experience has been with severe brain injuries; thus, it is not surprising that the first results are undramatic.—*A. Franklin Turner, M.D.*

Neck and Chest

HERS, J. F. P. Clinical aspects of infection with Mycoplasma pneumoniae. *Proc. Roy. Soc. Med.*, Dec., 1968, *61*, 1325–1330. (From: The Department of Clinical Respiratory Virology, University Hospital, Leiden, The Netherlands.)

Mycoplasma pneumoniae is thought to be the etiologic agent of primary atypical pneumonia.

The symptomatology, physical findings, laboratory findings, roentgenology, treatment and complications are discussed.

The roentgenographic abnormalities are not characteristic. The chest roentgenogram may be normal or may show areas of infiltration. These areas vary considerably in location and intensity.—*Richard P. Taylor, M.D.*

SURPRENANT, E., WILSON, A., BENNETT, L., O'REILLY, R., and WEBBER M. Changes in regional pulmonary function following bronchography. *Radiology*, Oct., 1968, *91*, 736–741. (From: Department of Radiology, UCLA Center for the Health Sciences, Los Angeles, Calif. 90024.)

The impetus to pursue this study was provided by a random perfusion lung scan performed the same day, but following bronchography. When compared to a prior scan new defects were apparent. A concurrent chest roentgenogram revealed residual contrast medium in the bronchi. Were the perfusion defects due to infarcts or the result of bronchography? The results of previous investigators seemingly lent substance to the latter as causative agent: (1) spirometric and blood gas studies show impaired pulmonary function during bronchography with rapid improvement following expectoration; (2) impaired lung volume seems to be due, to some degree, to bronchial obstruction by contrast media; (3) experimentally, perfusion of a segment of lung can be impaired by depleting it of alveolar oxygen; and (4) acute and perennial asthma patients show abnormal pulmonary perfusion patterns, probably due to airway narrowing.

The techniques employed were: (1) routine bronchography with 10–40 ml. dionosil (oily propyliodone); (2) posterior and lateral perfusion lung scans with 1.5–2.0 mc MAA-Tc^{99m}, upright on gamma camera and supine on rectilinear scanner; (3) posterior and lateral ventilation lung scans with 2 mc Xe^{133} in normal tidal volumes of air, upright on gamma camera; and (4) routine chest roentgenography concurrent with other procedures.

Eight of the 9 patients studied by bronchography had perfusion scans prior to bronchography, and 1 of these also had a prior ventilation scan. Five of these 8 had repeat scans 1 hour after bronchography and 2 had repeat scans 1 day after bronchography. The eighth patient had 2 bronchographies, and was rescanned 1 day after the first and 1 hour after the second. The ninth had ventilation and perfusion scans after bronchography only.

All patients studied 1 hour after bronchography showed new perfusion defects which related well to the distribution of residual propyliodone on the chest roentgenograms. The perfusion pattern on the studies performed 1 day after bronchography revealed no new perfusion defects, and 1 even appeared improved over the baseline study. This latter phenomenon is presumed to be due to the elimination of mucus plugs by coughing which was initiated by an unsatisfactory bronchography. The companion ventilation scans showed similar defects to the perfusion scan studies.

It would seem that lung scans can be adversely (artefactitiously) affected by partial bronchial obstruction whether due to bronchographic media, mucus plugs, or other causes.—*F. C. Petty, M.D.*

COOLEY, DENTON A., and HALLMAN, GRADY L.

Surgical treatment of left ventricular aneurysm: experience with excision of postinfarction lesions in 80 patients. *Prog. Cardiovasc. Dis.*, Nov., 1968, *11*, 222–228. (From: The Cora and Webb Mading Department of Surgery, Baylor University College of Medicine and the Texas Heart Institute of St. Luke's Episcopal and Texas Children's Hospital, Houston, Texas.)

Left ventricular aneurysm is a serious complication of myocardial infarction and lessens the chances of survival. Paradoxical motion of the aneurysm reduces left ventricular output and may result in intractable heart failure. Embolization from mural thrombus is an ever present hazard. The diagnosis of an aneurysm can be readily established and the severity of cardiac impairment assessed by clinical means. The timing of the operation is important. Adequate fibrous tissue must be formed about the aneurysm so that sutures may be placed firmly and not in friable myocardium. The authors believe that 2 or 3 months should be the minimum interval between myocardial infarction and the removal of ventricular aneurysm in order to allow sufficient scar to form in the surrounding myocardium.

Utilizing a cardiopulmonary bypass the perfusion is conducted at normothermia. The technique of the operation is described in detail. Between January 1958, and March, 1968, at Baylor University College of Medicine, 80 patients underwent operation for removal of postinfarction aneurysm of the left ventricle. There was a 20 per cent mortality rate. A significant decrease in the cardiac silhouette was observed in all of the patients and none of the aneurysms recurred during a follow-up period that extends to 10 years for the longest survivor. Satisfactory rehabilitation of the survivors was achieved.

It is felt that in spite of advances in techniques of perfusion and surgery, patients with extensive muscular damage would not survive operation. In these patients the principal hope lies in the possibilities for cardiac transplantation.—*S. A. Kaufman, M.D.*

Abdomen

Burhenne, H. Joachim. The iatrogenic afferent-loop syndrome. *Radiology*, Nov., 1968, *91*, 942–947. (From: Children's Hospital and Adult Medical Center, 3700 California Street, San Francisco, Calif. 94119.)

The afferent-loop syndrome is caused by obstruction in either the proximal or the distal jejunal limb close to the gastrojejunostomy. Scarring, neoplasm, intussusception, twisting, or internal herniation may also play a part in causing this syndrome. The author presents in this paper a different cause for obstruction which occurs in the distal jejunal limb just beyond the anastomosis and results from a poorly constructed gastrojejunostomy. This afferent-loop syndrome occurs more frequently with surgical construction of a partial stoma and with a left-to-right anastomosis. The partial obstruction usually occurs in the distal jejunal limb just beyond its attachment to the lesser curvature and causes stasis and distention of the proximal duodenojejunal loop with gastric reflux of food mixed with biliary and pancreatic secretions.

Eight patients with a left-to-right gastrojejunostomy and who had the afferent-loop syndrome are discussed by the author. This diagnosis is suggested when contrast medium reveals distention of the proximal loop and retention of the medium in this loop on 60 minute roentgenograms. Careful fluoroscopy is necessary to identify the proximal and distal limbs, and the distended proximal duodenojejunal loop will be found in a more posterior position and best seen with the patient erect. The fluoroscopic findings include the presence of deep contractions in the distended limb with regurgitation of contrast material into the stomach. Only a small amount of medium passes in a forward direction through the angulated distal limb at the lesser curvature aspect. It is suggested that a mixture of food and barium is more diagnostic for the actual degree of obstruction.

It is the author's opinion that the diagnosis of the iatrogenic afferent-loop syndrome is made roentgenologically with careful fluoroscopy, and appropriate roentgenograms and that delayed roentgenographic examination is essential during the investigation.—*Donald N. Dysart, M.D.*

Goulston, Kerry, and Cooke, Allan R. Alcohol, aspirin, and gastrointestinal bleeding. *Brit. M. J.*, Dec. 14, 1968, *4*, 664–665. (From: A. W. Morrow Department of Gastroenterology, Royal Prince Alfred Hospital, Sydney, Australia.)

The authors report the investigation of gastrointestinal blood loss after the ingestion of aspirin alone, alcohol alone, and aspirin and alcohol.

The blood loss was measured by tagging the red blood cells with chromium 51 and determining its presence in the stool.

Alcohol alone did not cause gastrointestinal bleeding, but it did increase aspirin-induced blood loss.—*Richard P. Taylor, M.D.*

Hamilton, J. R. Seat-belt injuries. *Brit. M. J.*, Nov. 23, 1968, *4*, 485–486. (From: Lurgan and Portadown Hospital, Lurgan, County Armagh, N. Ireland.)

This article re-emphasizes that injuries often occur even with the use of seat belts in automobile accidents.

The 4 patients in this report were wearing not only the lap belt, but also the diagonal extension. Intra-abdominal injuries may be present without

associated external marks and with minor complaints. Perforated bowel may have an insidious course and a poor prognosis.

The author suggests that bruising of the anterior abdominal wall or the continued presence of even slight abdominal pain without visible injury should be an indication for exploratory laparotomy. Three of his 4 patients had perforation of the small bowel diagnosed and treated 30 hours, 4 days and 6 days after injury; the latter also had a tear of the splenic capsule.

The patients had very little pain and only slight abdominal distention and tenderness, which was aggravated just before surgery. Two patients had fracture-dislocations of the spine.—*Martha Mottram, M.D.*

GENITOURINARY SYSTEM

CRUESS, RICHARD L., BLENNERHASSETT, JOHN, MACDONALD, F. ROBERT, MACLEAN, LLOYD D., and DOSSETOR, JOHN. Aseptic necrosis following renal transplantation. *J. Bone & Joint Surg.*, Dec., 1968, *50A*, 1577–1590. (From: The Royal Victoria Hospital and McGill University, Montreal, Quebec, Canada.)

As experience accumulates with organ transplantation, it becomes apparent that there are risks involved to the tissues in the recipient other than the transplanted organ. One of these complications is aseptic necrosis which is being recognized more frequently.

In this series from the Royal Victoria Hospital in Montreal there was a total of 27 patients who survived renal transplantation for 6 months or more. Ten patients were diagnosed as having aseptic necrosis. Cadaver kidneys had been used in all patients and a standard operative procedure followed. The regime for postoperative immunosuppression was uniform utilizing azathioprine, steroids, and actinomycin C.

Nine patients demonstrated aseptic necrosis of the femoral head, 5 had involvement of the hips alone, 5 showed aseptic necrosis of the knee joint, and 2 had a lesion of the humeral head. The average time after the transplantation when symptoms arose was 7 months and the roentgen changes usually were seen 2 months later. The roentgenographic manifestations were quite uniform. In the femoral head and humeral head there was subchondral demineralization, at first patchy but tending to extend, remaining however fairly well demarcated. In some cases there was collapse of the bone and in others there was some remineralization and healing. The roentgenologic changes about the knee showed involvement of the femur and tibia but it did not begin in the subchondral area. There was patchy demineralization but no gross evidence of collapse was seen. One patient showed osteochondritis dissecans in addition to the other findings. Joint effusion was frequent. Eight of the ten patients were treated non-operatively with supportive measures only.

The etiology of these lesions is speculated upon; the role of the immunosuppressive drugs and the high doses of cortical steroids that are used should be considered. The two most likely explanations are concerned with steroid-induced osteoporosis and fat embolization. It has been shown that fat tends to accumulate in the liver of cortisone-treated individuals which may give rise to fat emboli. A steroid induced vasculitis would seem a less plausible explanation.

Dr. James S. Miles in his discussion of this paper notes that in his series of 190 transplantation patients there have been 2 patients who died of lymphoma. He believes that the production of such a malignant tumor may be related to the antilymphocyte serum or to the prolonged suppression of the immune response.—*S. A. Kaufman, M.D.*

KLOTZ, P. G. Ureteral reflux in adults. *Canad. M. A. J.*, Jan. 4, 1969, *100*, 4–12. (Address: Suite 609, 99 Avenue Road, Toronto 5, Ontario, Canada.)

In children, ureterovesical reflux is present in 75 per cent of patients with recurrent urinary tract infection. "Voiding cystography" is mandatory in the urologic investigation of these patients.

Ureteral reflux is being detected with increasing frequency in adults, both male and female, and this diagnostic procedure is also necessary in the assessment of the adult urinary tract. The majority of adults with recurrent urinary tract infection do not have reflux but its presence should be excluded.

Eight adult patients with ureteral reflux (6 females and 2 males) are reported. All of them had recurrent urinary tract infection for periods ranging from 2 months to 9 years and there was no other apparent etiologic factor. Intravenous pyelography was normal unless a significant degree of pyelonephritis or ureteritis had developed. Voiding cystography demonstrated ureteral reflux. Conservative treatment with long-term chemotherapy is rarely successful in the adult patient with ureterovesical reflux and surgery is usually necessary. Reimplantation of the ureters is usually effective, but if pyelonephritic changes are advanced a partial or even total nephrectomy may be necessary.

The entity of ureterovesical reflux remains a puzzle; its etiology, its relationship to infection, the increased frequency in females, and the delay in onset of symptoms are as yet unexplained. It should be suspected in patients with recurring urinary tract infection and voiding cystography should be performed.—*S. A. Kaufman, M.D.*

HASSIM, ABU M., CARRUTHERS, R. H., and LUCAS, CYNTHIA. Bilharzial contracted blad-

der treated by ileocystoplasty. *Brit. J. Surg.*, Sept., 1968, *55*, 703–705. (From: Lusaka Central Hospital, Zambia, Africa.)

Schistosoma haematobium infestation of the urinary tract involves mainly the lower ureters and bladder. The majority of lesions occur around the ureteric orifices, trigone and adjacent lateral walls of the bladder. Although lesions are not usually seen in the vault of the bladder during cystoscopy, their presence is demonstrated as generalized calcification of the bladder wall on roentgenographic examination.

Granulation tissue produced by ova deposition is followed by severe fibrosis which may lead to ureteral stricture and hydronephrosis. Bladder neck contraction may be produced by the fibrosis and lead to obstruction and bladder distention with ureteric reflux.

Two cases are reported which demonstrate diffuse involvement producing total bladder contraction and incontinence. Whereas in cases of simple obstruction vesical cervicoplasty usually suffices, in these cases ileocystoplasty was performed and was followed by return of control of micturition and improvement of renal function. The anastomoses healed by first intention despite heavy infestation in the area. Inasmuch as these patients are subject to recurrent pyelonephritis, sulfonamide prophylaxis is recommended.

In patients with a bladder capacity of less than 250 ml., ileocystoplasty has been recommended. Honey and Gelfand have reported 8 such procedures.

A full term normal pregnancy was delivered in one of the patients in the current study a year after the surgery, demonstrating the compatibility of successful pregnancy with the postoperative state.—*Major Edward Savolaine, MC*

Whitaker, J., and Johnston, G. S. Correlation of urethral resistance and shape in girls. *Radiology*, Oct., 1968, *91*, 757–761. (From: The Royal Children's Hospital, Flemington Road, Parkville, Victoria 3052, Australia.)

An objective study of the shape of the urethra was done on 60 females, ages 4 to 14 years except 1 patient who was 22 years of age.

A urodynamic approach was used, measuring the bladder pressure (P_B) after introducing diaginol until a desire for voiding was obtained. A suprapubic needle was passed into the bladder under a local anesthetic for bladder pressure measurement. The equivalent exit pressure (P_E) was obtained by placing a collecting funnel containing a tambour between the thighs just below the external urethral meatus. The urine was made to play onto the tambour and then collected giving the urinary flow rate (F). Resistance (R) was then calculated from the equation:

$$R = \frac{P_B - P_E}{F^2}.$$

Voiding was recorded by cineradiography or by plain roentgenography and the shape of the urethra was determined. This was done with the patient standing in an oblique position. The urethral shape was found to be, in order of frequency, cylinder, fusiform, arrowhead, cone, wineglass and string.

In the cylinder, fusiform, arrowhead and the cone-shaped urethras the upper limit of normal was found to be 0.07 mm. Hg/ml.^{2}/sec. In the wineglass and string-shaped urethras the resistance was greater than 0.07 mm. Hg/ml.^{2}/sec. in every case. Voluntary controlled micturition in 4 of the 7 patients with elevated resistance, not organic abnormality of the urethra, was responsible for the urethral narrowing and elevated resistance, according to the authors.—*C. T. Edmondson, M.D.*

RADIATION THERAPY

Davidson, J. W., and Renouf, J. H. P. Radiographic findings in "Burkitt type" lymphoma. *J. Canad. A. Radiologists*, Sept., 1968, *19*, 121–125. (From: The Department of Radiodiagnosis, The Ontario Cancer Institute and University of Toronto, Toronto, Ontario, Canada.)

The authors report the case of a 5½ year old boy with an anterior superior mediastinal mass associated with irregular narrowing of the descending colon and a left flank mass. Lymphography demonstrated numerous enlarged, irregularly filled lymph nodes in the retro and supraclavicular areas. The para-aortic and pelvic lymph node architecture appeared normal. Biopsy of a palpable left supraclavicular lymph node showed an undifferentiated type of lymphocytic lymphoma, with "isolated phagocytic histiocytes with 'starry sky' appearance and primitive lymphocytic cells consistent with Burkitt lymphoma."

A high incidence of abdominal tumors has been reported in the larger series of "Burkitt lymphoma." One hundred and twenty-one cases of children with malignant lymphoma exclusive of Hodgkin's disease at the Ontario Cancer Institute were reviewed and no case could be found in which the presenting site was the descending colon. Sixty per cent of the patients in this series showed a generalized distribution of lymphographic findings characteristic of lymphosarcoma, with homogeneous even granulation, in contrast to the case reported, which demonstrated normal pelvic and para-aortic lymph node architecture, and irregularly filling supraclavicular lymph nodes more resembling Hodgkin's disease of mixed cellularity and reticulum cell sarcoma.

The roentgenographic findings in this case may be important evidence of a disease entity with histologic features of "Burkitt lymphoma," and demonstrate the value of comprehensive roentgenographic investigation of such patients.—*William Lynch, M.D.*

CHEMOTHERAPY

Cohn, Isidore, Jr., Slack, Nelson H., and Fisher, Bernard. Complications and toxic manifestations of surgical adjuvant chemotherapy for breast cancer. (New Orleans, La.; Buffalo, N. Y.; and Pittsburgh, Pa.) *Surg., Gynec. & Obst.*, Dec., 1968, *127*, 1201–1209.

Since 1957, 45 institutions have participated in cooperative clinical trials to evaluate the worth of chemotherapy as an adjunct to the Halsted method of radical mastectomy in treatment of cancer of the female breast. In a Phase 1 protocol, patients were randomized in a double blind manner, so that they received Thio-tepa (or TSPA) or a placebo the day of and for 2 successive days after operation.

A new study, Phase 2, was begun to determine the value of fluorouracil (5-FU) compared to triethylenethiophosphoramide as an adjunct to operation and to compare, or deny, the effects of triethylenethiophosphoramide being observed in the Phase 1 study. In addition, the Phase 2 program is continuing to evaluate postoperative radiotherapy and prophylactic oophorectomy.

The authors analyze, in detail, the surgical complications and toxic manifestations encountered in the Phase 2 study resulting from the employment of triethylenethiophosphoramide, fluorouracil, or a placebo in 1,328 patients.

Surgical services of 36 universities or cancer institutes contributed patients to the Phase 2 study. Patients between 30 and 75 years of age were considered eligible for inclusion if they had a potentially curable cancer of the breast.

Results. Platelet and white blood cell counts were obtained after operation at least once each week for 4 successive weeks.

Administrations of fluorouracil resulted in the greatest decrease of the white blood cell count. Approximately 42 per cent of patients had a white blood cell count within the leukopenic range and nearly half of these were below 2,500. Two groups of patients that received triethylenethiophosphoramide exhibited an identical decrease of white blood cell count. About 15 per cent were in the leukopenic range.

Platelet counts were unaffected by either triethylenethiophosphoramide or fluorouracil therapy.

More than 40 per cent of patients who underwent radical mastectomy and received a placebo had some undesirable local surgical sequela. Postmenopausal patients in this group had a 14 per cent higher complication rate than did the premenopausal patients. When fluorouracil was administered, the complication rate was significantly higher than it was for the placebo group.

Premenopausal patients receiving fluorouracil suffered the most undesirable local effects. Fifty per cent of such patients had complications—a significantly greater number than was observed in either premenopausal triethylenethiophosphoramide or placebo groups.

It was disturbing to find that about 20 per cent of the patients suffered wound infections after radical mastectomy, whether or not chemotherapy was administered.

A high incidence of fever and nausea occurring in patients of the chemotherapy groups is certainly noteworthy. Both chemical groups were similar in this regard.

A high degree of toxicity encountered with fluorouracil is strikingly evident, as is the prolongation of symptoms in many patients.

Fluorouracil in the dosage given, when used in conjunction with operation, resulted in an unacceptable incidence of hemic, local, and systemic complications, as well as occasional deaths associated with drug toxicity. Occurrence of such findings could, at best, only be justified if the antitumor effect of the treatment was striking. Since that has failed to materialize, further use of fluorouracil in the regimen used as an adjunct to operation in the treatment of breast cancer is not justified and may be challenged.

The studies emphasize that the worth of surgical adjuvant chemotherapeutic agents for breast cancer remains to be proved by clinical experimental trials. Their use is not totally without hazard.—*Stephen N. Tager, M.D.*

SUBJECT INDEX TO VOLUME 105

(E) = editorial (ab) = abstract

Abdominal aorta, calcification of, and osteoporosis of lumbar vertebrae in women living in Durban (ab), 478
stab wounds, injection of hypaque (sodium diatrizoate) in management of (ab), 476
Adenocarcinoma of endometrium, combination of external irradiation and curietherapy used preoperatively in, 586
of uterus, 603
Afterloading, vaginal ovoids, 609
Air, significance of, in biliary system and liver (ab), 716
Alcohol, aspirin, and gastrointestinal bleeding (ab), 934
American Radium Society, Fifty-first Annual Meeting of (E), 208
preliminary program, 212
Ampulla of Vater and chronic pancreatitis, significance of intravenous cholangiography associated with duodenography in study of (ab), 239
Amyloidosis and juvenile rheumatoid arthritis, extensive vascular calcification in association with (ab), 718
of bronchus resembling carcinoma (ab), 713
Aneurysm, left ventricular, surgical treatment of, experience with excision of postinfarction lesions in 80 patients (ab), 933
Aneurysms of superficial temporal artery, 331
posterior fossa, presenting as mass lesions, 334
Angiocardiography, effect of, on fluid and electrolyte balance, 777
Angiographic and catheterization findings in patients with difficulties after total correction of tetralogy of Fallot (ab), 235
appearance, unusual, of cerebral arteriovenous malformations, 326
demonstration of coarctation of aorta and similar anomalies (ab), 932
manifestations of Wilms' tumor; observation of six cases, 95
sign of persistent ductus arteriosus (ab), 720
Angiography and nephrotomography, role of: renal tuberculosis (ab), 241
and scintigraphy, comparison of findings by, in pulmonary pathology (ab), 235
contrast-vasoconstrictor mixtures in, 772
selective superior mesenteric, leiomyosarcoma of small bowel demonstrated by (ab), 715
Antrum, maxillary, lamina dura (L. D.) of: its value in roentgen diagnosis, 830
Aorta, coarctation of, and similar anomalies, angiographic demonstration of (ab), 932
Appendiceal disease, acute, use of barium in diagnosis of: new radiological sign (ab), 715
Arachnoid cysts, congenital, 298
Arterial hypertension, renal, excretory urogram in (ab), 242
Arteriography, coronary, in hypercholesterolemic patients, 784
counter-current, addition to technique of (ab), 247
renal, and isotope renography in evaluation of renal transplants, 682
selective bronchial, in demonstration of abnormal systemic circulation in lung (ab), 714
Arteriovenous, cerebral, malformations, unusual angiographic appearance of, 326
malformation, congenital, of foot, 877
Arthritis, juvenile rheumatoid, and amyloidosis, extensive vascular calcification in association with (ab), 718
spontaneous axial subluxation in child as first sign of (ab), 718
Arthur C. Singleton, M.D., 1900–1968 (E), 210
Asbestos, effects of, in dockyard workers (ab), 234
Aspirin, alcohol, and gastrointestinal bleeding (ab), 934
Atherosclerotic stenosis, transluminal dilatation of (ab), 246
Atomic bombings of Hiroshima and Nagasaki, breast cancer after exposure to (ab), 484
Aubrey Otis Hampton lecture, 1968; lung: challenge of nuclear medicine, 251
A.U.R., winds of change pass over (E), 919
Autotomography applied to pharynx and dens; simple wand for technique, 359
Axis, foramen transversarium, roentgenographic examination of; practical considerations, 361
Azygography, pre and postirradiation: its value in determining surgical resectability in pulmonary carcinoma, 83

Barium, use of, in diagnosis of acute appendiceal disease; new radiological sign (ab), 715
Beam therapy, external, radiation induced neoplasia following, for children with retinoblastoma, 529
Biliary system and liver, significance of air in (ab), 716
Biopsy, stereotaxic transsphenoidal, and cryosurgery of pituitary tumors, 273
Bladder, bilharzial contracted, treated by ileocystoplasty (ab), 935
Blood, effect of parabens on permeability of: brain barrier to water-soluble radiopaque media, 404

Bone, calvarial, defects in neurofibromatosis; case report, 319
density, roentgenographic, use of digital computer in measurement of, 870
effect of direct current on (ab), 244
necrosis in joint disease (ab), 480
scans, radioisotope, response to radiation therapy of osseous lesions detected on, 137
some features of Paget's disease of, studied by stain historadiography (ab), 478
temporal, in Paget's disease, tomography of, 838
Book Reviews:
Radiographic Positioning and Related Anatomy. By Isadore Meschan, with assistance of R. M. F. Farrer-Meschan, 220
Surgical and Allied Malpractice. By Bernard J. Ficarra, 462
Physical and Photographic Principles of Medical Radiography. By Herman E. Seemann, 462
The Human Bronchial Circulation in Health and Disease. By Leon Cudkowicz, 703
Bowel, evisceration of, through vagina following irradiation for cervical carcinoma: report of first known cases (ab), 483
perforation of, in newborn as complication of exchange transfusion (ab), 715
small, leiomyosarcoma of, demonstrated by selective superior mesenteric angiography (ab), 715
spontaneous perforation of, in newborn following exchange transfusion (ab), 476
Brachial plexus, roentgen findings in obstetrical injuries to (ab), 240
Brain barrier to water-soluble radiopaque media: effect of parabens on permeability of blood, 404
lipid embolism to, following lymphography; case report and experimental study, 763
scanning, serial, with technetium 99m pertechnetate in cerebral infarction, 728
tumors, scintigraphy with ^{203}Hg and ^{99m}Tc in diagnosis of (ab), 473
Breast cancer after exposure to atomic bombings of Hiroshima and Nagasaki (ab), 484
cancer, complications and toxic manifestations of surgical adjuvant chemotherapy for (ab), 937
lesions, modified technique of ultrasonography for detection and differential diagnosis of, 446
Breathing, oxygen, and radiation therapy, changing perspectives in, 665
Bronchial arteriography, selective, in demonstration of abnormal systematic circulation in lung (ab), 714
Bronchography, changes in regional pulmonary function following (ab), 933
Bronchopulmonary dysplasia: radiographic features of pulmonary oxygen toxicity in newborn (ab), 234
Bronchus, amyloidosis of, resembling carcinoma (ab), 713
B-scan ultrasound exploration of neoplastic disease, 428
Bullosa, dystrophic epidermolysis; tolerance of bed and response of multifocal squamous cell carcinomas to ionizing radiation: report of case, 644
"Burkitt type" lymphoma, radiographic findings in (ab), 936

Calcification, extensive vascular, in association with juvenile rheumatoid arthritis and amyloidosis (ab), 718
of abdominal aorta and osteoporosis of lumbar vertebrae in women living in Durban (ab), 478
of posterior longitudinal ligament: cause of cervical myelopathy, 365
triangular cartilage, in wrists: its incidence in elderly persons, 850
Calculi of choledochus, radiologic findings in (ab), 476
Calvarial bone defects in neurofibromatosis; case report, 319
"doughnut lesion": previously undescribed entity, 314
Calyceal dilatation, isolated upper pole, significance of (ab), 717
Cancer, advanced, of head and neck, combined intra-arterial infusion and radiotherapy for treatment of, 20
breast, after exposure to atomic bombings of Hiroshima and Nagasaki (ab), 484
breast, complications and toxic manifestations of surgical adjuvant chemotherapy for (ab), 937
cell, HeLa, patterns of protein synthesis in, 746
early, of uterine cervix, simple modification of Stockholm applicator for treatment of, 115
esophageal, value of radiotherapy in management of (ab), 500
mammary, use of gamma camera for early detection of osseous metastases from (ab), 245
of base of tongue; 116 patients treated radiotherapeutically in 11 year period 1952 through 1962, 26
of corpus uteri, recurrent; techniques and results of treatment, 596
of esophagus, some opinions on treatment of, 514
of eye and surrounding structures, treated with radiation therapy, long time survivals of patients with, 566
of thoracic esophagus, surgical and radiation treatment of, 523

services, centralization of,—how far should it go? Janeway lecture, 1968, 487
Candida esophagitis (ab), 712
Carcinoma, amyloidosis of bronchus resembling (ab), 713
cervical, evisceration of bowel through vagina following irradiation for: report of first known case (ab), 483
of anterior nasal cavity, radiation therapy of, 550
of cervix, evaluation of Manchester system of treatment of, 579
of endometrium, progestogens in treatment of (ab), 250
of ovary, role of preoperative irradiation in treatment of, 614
of uterine cervix, new rectal dosimetry catheter for use in radiation therapy of, 120
pulmonary, its value in determining surgical resectability in: pre and postirradiation azygography, 83
uterine, radium dosage patterns in treatment of, 110
Carcinomas, multifocal squamous cell, tolerance of bed and response of, to ionizing radiation; dystrophic epidermolysis bullosa: report of case, 644
Carpal-tunnel syndrome, pseudogout, and hyperparathyroidism: case report (ab), 719
Cartilage, triangular, calcification in wrists: its incidence in elderly persons, 850
Cartilaginous tumors of base of skull, 308
Catheter, detached intravascular, or guide wire fragments, recovery of; proposed method, 894
new rectal dosimetry, for use in radiation therapy of carcinoma of uterine cervix, 120
Catheterization and angiographic findings in patients with difficulties after total correction of tetralogy of Fallot (ab), 235
selective third ventricular, for pantopaque ventriculography, 348
Cell cycle *in vivo*, radiation response in relation to, 734
Cerebral arteriovenous malformations, unusual angiographic appearance of, 326
infarction, serial brain scanning with technetium 99m pertechnetate in, 728
Cerebrospinal fluid formation, roentgenologic studies of, in dog, 756
rhinorrhea studied with gamma scintillation camera (ab), 483
Cerebrovascular diseases, occlusive, thermography in (ab), 231
Cervical carcinoma, evisceration of bowel through vagina following irradiation for: report of first known case (ab), 483
lymph node metastasis, management of, by megavoltage radiotherapy, 74
myelopathy, cause of: calcification of posterior longitudinal ligament, 365
spine, neurologic complications of Paget's disease, 375
spondylosis, roentgenographic correlations in, 370
Cervix, carcinoma of, evaluation of Manchester system of treatment of, 579
uterine, carcinoma of, new rectal dosimetry catheter for use in radiation therapy of, 120
uterine, early cancer of, simple modification of Stockholm applicator for treatment of, 115
*Child and young adult, acquired spondylolysis in: report of two cases (ab), 719
irradiated, osteosarcoma in—case report (ab), 479
spontaneous axial subluxation in, as first sign of juvenile rheumatoid arthritis (ab), 718
Childhood, surgical management of solid tumors in, 105
Children, idiopathic pulmonary hemosiderosis in (ab), 232
treatment and prognosis of medulloblastoma in; study of 82 verified cases, 43
with retinoblastoma, radiation induced neoplasia following external beam therapy for, 529
Cholangiography, drip infusion (ab), 238
intravenous, associated with duodenography, significance of, in study of ampulla of Vater and chronic pancreatitis (ab), 239
percutaneous transhepatic: study of 115 cases (ab), 239
Choledocus, calculi of, radiologic findings in (ab), 476
Chordoma, unusual manifestation of: report of two cases (ab), 717
Clavicle, congenital pseudoarthrosis of (ab), 718
Cobalt 60 rotational therapy, dosimetric considerations in, for esophageal lesions; comparison of transit and intraluminal dose measurement, 518
Coccidioides immitis, solitary pulmonary lesion due to (ab), 474
Coccidioidomycosis, pulmonary (ab), 474
Colchicine, mechanism of vitamin B_{12} malabsorption in patients receiving (ab), 237
Colonic perforation after exchange transfusion (ab), 716
Computer, digital, use of, in measurement of roentgenographic bone density, 870
dosimetry, clinical application of, in interstitial radium therapy, 165
Containers, radium, plugging of leaks in, 689
Contrast-vasoconstrictor mixtures in angiography, 772

Coronary arteriography in hypercholesterolemic patients, 784
Corpus uteri, cancer of, recurrent; techniques and results of treatment, 596
Cryosurgery and stereotaxic transsphenoidal biopsy of pituitary tumors, 273
Curietherapy and external irradiation, combination of, used preoperatively in adenocarcinoma of endometrium, 586
Cystitis, hemorrhagic radiation (ab), 482
Cystourethrography in University Hospital of West Indies (ab), 243
Cysts, congenital arachnoid, 298
post-traumatic leptomeningeal, 305
suprasellar subarachnoid; radioclinical features, 291

Dactinomycin therapy, single *versus* multiple dose, of Wilms' tumor (ab), 249
Dens and pharynx, autotomography applied to; simple wand for technique, 359
Dermoids and epidermoids, intraspinal, 386
Diabetic osteopathy, roentgen observations in (ab), 248
Diabetics, evaluation of peripheral circulation in, by means of modified radioisotopic technic (ab), 248
Diaphragm, traumatic rupture of, after blunt injury (ab), 236
Disease, malignant, of facial structures, interstitial radiation in management of, 14
Dosimetric and biologic problems posed by electron beam therapy, 178
considerations in cobalt 60 rotational therapy for esophageal lesions; comparison of transit and intraluminal dose measurements, 518
problem, technique and note on: roentgencinevideography (ab), 476
Dosimetry catheter, rectal, new, for use in radiation therapy of carcinoma of uterine cervix, 120
computer, clinical application of, in interstitial radium therapy, 165
telecobalt split field; with special reference to central penumbral isodose separation, 152
"Doughnut lesion," calvarial: previously undescribed entity, 314
Ductus arteriosus, persistent, angiographic sign of (ab), 720
Duodenography, significance of intravenous cholangiography associated with, in study of ampulla of Vater and chronic pancreatitis (ab), 239
Dyschondrosteosis, familial, new observation of (ab), 479
Dysostosis, epiphyseal, 860
Dystrophic epidermolysis bullosa; tolerance of bed and response of multifocal squamous cell carcinomas to ionizing radiation: report of case, 644

Echoencephalography in management of patients receiving radiation therapy (ab), 249
Echographic diagnosis of retroperitoneal lymph node enlargement; ultrasound scanning technique and diagnostic findings, 438
Echography, who should do? (E), 454
Editorials:
The Fifty-first Annual Meeting of the American Radium Society, 208
Arthur C. Singleton, M.D., 1900–1968, 210
Who Should Do Echography?, 454
W. Walter Wasson, M.D., 1884–1968, 456
The Reynolds Historical Library, 699
Winds of Change Pass Over the A. U. R., 919
Palmer E. Wigby, M.D., 1903–1968, 921
Electrode placement technics in electroencephalography, role of neuroroentgenology in (ab), 231
Electroencephalography, role of neuroroentgenology in electrode placement technics in (ab), 231
Electrolyte and fluid balance, effect of angiocardiography on, 777
Electron beam, 6–18 mev., current techniques with, 172
therapy, dosimetric and biologic problems posed by, 178
Embolism, lipid, to brain following lymphography; case report and experimental study, 763
Emphysema, (lobar), congenital and localized (ab), 473
Endometrium, adenocarcinoma of, combination of external irradiation and curietherapy used preoperatively in, 586
carcinoma of, progestogens in treatment of (ab), 250
Energy, low, and long half-life radiation sources, permanent interstitial therapy using, 157
Epidermoids and dermoids, intraspinal, 386
Epidermolysis bullosa, dystrophic; tolerance of bed and response of multifocal squamous cell carcinomas to ionizing radiation: report of case, 644
Epidural spinal hemorrhage, spontaneous, 383
Epiphyseal dysostosis, 860
Epithelium, small intestinal, of dogs, enhancement of x-ray effects on, by Actinomycin D, 126
Esophageal cancer, value of radiotherapy in management of, 500
lesions, dosimetric considerations in cobalt 60 rotational therapy for; comparison of transit and intraluminal dose measurements, 518
Esophagitis, *Candida* (ab), 712
Esophagus and pharynx, evaluation of radiopacity

of various ingested foreign bodies in (ab), 713
cancer of, some opinions on treatment of, 514
smooth-muscle tumors of (ab), 236
thoracic, cancer of, surgical and radiation treatment of, 523
Extravasates with intravenous urography (ab), 241
Eye and surrounding structures, cancer of, treated with radiation therapy, long time survivals of patients with, 566

Facial structures, interstitial radiation in management of malignant disease of, 14
Fahr's disease, idiopathic familial cerebrovascular ferrocalcinosis, and review of differential diagnosis of intracranial calcification in children, 352
Fetal death, radiologic diagnosis of (ab), 240
Fifty-first Annual Meeting of American Radium Society (E), 208
preliminary program, 212
Fluid and electrolyte balance, effect of angiocardiography on, 777
formation, cerebrospinal, roentgenologic studies of, in dog, 756
Foot, congenital arteriovenous malformation of, 877
Foramen tranversarium of axis, roentgenographic examination of, practical considerations, 361
Foreign bodies, various ingested, in pharynx and esophagus, evaluation of radiopacity of (ab), 713
Fractures, seat belt: report of two cases (ab), 244
Friedländer's bacilli, radiologic findings in pneumonia caused by; as noted in 62 cases (ab), 232

Gamma camera, use of, for early detection of osseous metastases from mammary cancer (ab), 245
labeled active-site-directed enzyme inhibitor: ^{131}I-3′-iodoaminopterin (ab), 484
scintillation camera, cerebrospinal fluid rhinorrhea studied with (ab), 483
Gastric filling defects, small, significance of (ab), 475
Gastrointestinal bleeding, alcohol, and aspirin (ab), 934
Gastropathy, radiologic appearance of, with giant plicae (Ménétrier's disease) (ab), 475
Genetic counseling and physician (ab), 484
Girls, correlation of urethral resistance and shape in (ab), 936
Glioblastomas, vascular structures of, 795
Goldenhar's syndrome (oculoauriculovertebral dysplasia), roentgenological aspects of (ab), 230
Guide wire fragments, recovery of detached intravascular catheter or; proposed method, 894

Hands, study of inter- and intra-observer error in reading plain roentgenograms of; "to err is human," 853
Head and neck, combined intra-arterial infusion and radiotherapy for treatment of advanced cancer of, 20
and neck, neoplasms of radiosensitizer in treatment of: hydroxyurea, 555
injury, severe, preliminary observations of external hydrocephalus after (ab), 932
HeLa cancer cell, patterns of protein synthesis in, 746
Hemorrhage, spontaneous epidural spinal, 383
Hip, vitallium mold arthroplasty of, roentgenologic and clinical evaluation of (ab), 481
Historadiography, stain, some features of Paget's disease of bone studied by (ab), 478
Hodgkin's disease and other malignant lymphomas, clinical course of, treated with radical radiation therapy, 618
basis for segmental sequential irradiation in: extended *vs.* local fields in radiocurability of SJL/J mouse Hodgkin's-like reticulum cell sarcoma, 806; clinical experience of patterns of recurrence, 814
curative treatment of, 629
Hyaline-membrane, clinical, residual pulmonary findings in (ab), 473
Hydatidiform mole, use of hysterography in detection of, 885
Hydrocephalus, external, preliminary observations of, after severe head injury (ab), 932
primary congenital: long term results of controlled therapeutic trial (ab), 712
Hydroxyurea: radiosensitizer in treatment of neoplasms of head and neck, 555
Hyoid apparatus, roentgenologic consideration of, 63
Hypaque (sodium diatrizoate), injection of, in management of abdominal stab wounds (ab), 476
Hypercholesterolemic patients, coronary arteriography in, 784
Hyperparathyroidism, primary, modern research on (ab), 479
pseudogout, and carpal-tunnel syndrome: case report (ab), 719
Hyperphosphatasia, congenital: clinical, pathological, and biochemical study of two cases (ab), 480
Hypo-hyperparathyroidism (ab), 244
Hypophosphatemia, adult nonfamilial, with severe osteomalacia, metabolic and orthopedic treatment of case of (ab), 245

Hysterography, use of, in detection of hydatidiform mole, 885

^{131}I-3′-iodoaminopterin: gamma labeled active-site-directed enzyme inhibitor (ab), 484
-hippuran, rapid sequential kidney scanning with (ab), 717
Iatrogenic afferent-loop syndrome (ab), 934
ICRU, International Commission on Radiation Units and Measurements, 215
Idiopathic familial cerebrovascular ferrocalcinosis (Fahr's disease) and review of differential diagnosis of intracranial calcification in children, 352
Ileocystoplasty, bilharzial contracted bladder treated by (ab), 935
Image enlargement scale for stereotactic surgery, 270
Independent radiation monitor (I.R.M.), 900
Infection with Mycoplasma pneumonia, clinical aspects of (ab), 933
Inferior vena cava and renal veins, thrombosis of, complicating lupus nephritis (ab), 477
International Commission on Radiation Units and Measurements (ICRU), 215
Interstitial radium therapy, clinical application of computer dosimetry in, 165
therapy, permanent, using low energy and long half-life radiation sources, 157
Intra-arterial infusion and radiotherapy, combined, for treatment of advanced cancer of head and neck, 20
Intracranial calcification, review of differential diagnosis of, and idiopathic familial cerebrovascular ferrocalcinosis (Fahr's disease), in children, 352
Ionization chamber, modulation transfer functions of, 185
I.R.M., independent radiation monitor, 900
Irradiation, basis for segmental sequential, in Hodgkin's disease: extended *vs.* local fields in radiocurability of SJL/J mouse Hodgkin's-like reticulum cell sarcoma, 806; clinical experience of patterns of recurrence, 814
external, and curietherapy, combination of, used preoperatively in adenocarcinoma of endometrium, 586
preoperative, role of, in treatment of carcinoma of ovary, 614
Isotope renography and renal arteriography in evaluation of renal transplants, 682
Isotopes, radioactive, skin exposure from handling syringes containing, 897

Janeway lecture, 1968; centralization of cancer services—how far should it go?, 487
Jejunal morphological characteristics in South Vietnamese residents: preliminary report (ab), 714

Joint disease, bone necrosis in (ab), 480

Kidney, medullary sponge, polycystic renal disease presenting as (ab), 240
scanning, rapid sequential, with ^{131}I-hippuran (ab), 717

Lamina dura (L. D.) of maxillary antrum: its value in roentgen diagnosis, 830
Larynx, immature rabbit, effects of ionizing radiation upon, 791
Leaks, plugging of, in radium containers, 689
Leiomyosarcoma of small bowel demonstrated by selective superior mesenteric angiography (ab), 715
Leptomeningeal cysts, post-traumatic, 305
Leukemia, plasma cell, spontaneous rupture of spleen in (ab), 716
Library, Reynolds Historical (E), 699
Ligament, posterior longitudinal, calcification of: cause of cervical myelopathy, 365
Light analog system for radiotherapy planning, 648
Liver and biliary system, significance of air in (ab), 716
transplantation, experimental and clinical orthotopic, radioisotope scanning in (ab), 237
"Local tumor extent-time," influence of relationship, upon evolution of tumors of nasopharynx, 536
Lumbar vertebrae, osteoporosis of, and calcification of abdominal aorta in women living in Durban (ab), 478
Lung: challenge of nuclear medicine; Aubrey Otis Hampton lecture, 1968, 251
selective bronchial arteriography in demonstration of abnormal systemic circulation in (ab), 714
Lupus nephritis, thrombosis of renal veins and inferior vena cava complicating (ab), 477
Lymph node, cervical, metastasis, management of, by megavoltage radiotherapy, 74
retroperitoneal, enlargement, echographic diagnosis of; ultrasound scanning technique and diagnostic findings, 438
Lymphography, lipid embolism to brain following; case report and experimental study, 763
mediastinal (ab), 482
Lymphoma, "Burkitt type," radiographic findings in (ab), 936
Lymphomas, malignant, clinical course of Hodgkin's disease and other, treated with radical radiation therapy, 618

Malaria, falciparum, acute pulmonary edema in: clinicopathological correlation (ab), 233
Malignant neoplasm, ^{99m}Tc pertechnetate scintiphotography as diagnostic and follow-up

aids in major vascular obstruction due to (ab), 247
Mammary cancer, use of gamma camera for early detection of osseous metastases from (ab), 245
Mammographic technique: need for routine spot roentgenograms, 880
Manchester system of treatment of carcinoma of cervix, evaluation of, 579
Maxillary antrum, lamina dura (L. D.) of: its value on roentgen diagnosis, 830
Medulloblastoma, treatment and prognosis of, in children; study of 82 verified cases, 43
twenty years' experience with radiation therapy of, 37
Megacolon, toxic (ab), 715
Megavoltage radiotherapy, management of cervical lymph node metastasis by, 74
Melorheostosis: report of clinical, roentgenographic, and pathological findings in fourteen cases (ab), 478
Ménétrier's disease, radiologic appearance of gastropathy with giant plicae (ab), 475
Meningocele, occult intrasacral, 390
Metastasis, cervical lymph node, management of, by megavoltage radiotherapy, 74
Mole, hydatidiform, use of hysterography in detection of, 885
Monitor, independent radiation, (I.R.M.), 900
Mycoplasma pneumonia, clinical aspects of infection with (ab), 933
Myelographic table, simple biplane, 411

Nasal cavity, anterior, radiation therapy of carcinoma of, 550
Nasopharynx, influence of relationship "local tumor extent-time" upon evolution of tumors of, 536
Neck and head, combined intra-arterial infusion and radiotherapy for treatment of advanced cancer of, 20
Necrosis, aseptic, following renal transplantation (ab), 935
Neoplasia, radiation induced, following external beam therapy for children with retinoblastoma, 529
Neoplastic disease, B-scan ultrasound exploration of, 428
Nephrotomography and angiography, role of: renal tuberculosis (ab), 241
Neurofibromatosis, calvarial bone defects in; case report, 319
Newborn, perforation of bowel in, as complication of exchange transfusion (ab), 715
radiographic features of pulmonary oxygen toxicity in; bronchopulmonary dysplasia (ab), 234
radioisotope renography in assessment of renal function in (ab), 242
spontaneous perforation of bowel in, following exchange transfusion (ab), 476
Nuclear medicine, challenge of: lung; Aubrey Otis Hampton lecture, 1968, 251

Obstetrical injuries to brachial plexus, roentgen findings in (ab), 240
Osseous lesions, response to radiation therapy of, detected on radioisotope bone scans, 137
Osteogenesis imperfecta, pathogenesis of (ab), 477
Osteomalacia, severe, metabolic and orthopedic treatment of case of adult nonfamilial hypophosphatemia with (ab), 245
Osteopathy, diabetic, roentgen observations in (ab), 248
Osteoporosis of lumbar vertebrae and calcification of abdominal aorta in women living in Durban (ab), 478
Osteosarcoma, histological and radiographical classification of, in relation to therapy: review of 245 cases located in extremities (ab), 482
in an irradiated child—case report (ab), 479
parosteal, 142
Ovary, carcinoma of, role of preoperative irradiation in treatment of, 614
Oxygen breathing and radiation therapy, changing perspectives in, 665

Paget's disease in cervical spine, neurologic complications of, 375
of bone, some features of, studied by stain historadiography (ab), 478
tomography of temporal bone in, 838
Palmer E. Wigby, M.D., 1903–1968 (E), 921
Pancreatitis, chronic, and ampulla of Vater, significance of intravenous cholangiography associated with duodenography in study of (ab), 239
Pantopaque ventriculography, selective third ventricular catheterization for, 348
Parabens, effect of, on permeability of blood: brain barrier to water-soluble radiopaque media, 404
Parathyroid hormone and thyrocalcitonin, role of: familial pseudohypoparathyroidism (ab), 718
Parosteal osteosarcoma, 142
Pelvimetry technique, and roentgenologic rule, 890
Peripheral circulation, evaluation of, in diabetics by means of modified radioisotopic technic (ab), 248
Pharynx and dens, autotomography applied to; simple wand for technique, 359
and esophagus, evaluation of radiopacity of various ingested foreign bodies in (ab), 713

Phlebography, occlusive, significance of, in evaluation of therapeutic portocaval anastomoses (ab), 246
orbital (ab), 230
Physician and genetic counseling (ab), 484
Pineal body, calcified, localization of, on lateral roentgenograms, 287
Pituitary tumors, stereotaxic transsphenoidal biopsy and cryosurgery of, 273
Planning, radiotherapy, light analog system for, 648
Pneumonia, Mycoplasma, clinical aspects of infection with (ab), 933
radiologic findings in, caused by Friedländer's bacilli; as noted in 62 cases (ab), 232
Portocaval anastomoses, therapeutic, significance of occlusive phlebography in evaluation of (ab), 246
Posterior fossa aneurysms presenting as mass lesions, 334
fossa, vascular malformations of, including tentorial hiatus, 341
longitudinal ligament, calcification of; cause of cervical myelopathy, 365
Progestogens in treatment of carcinoma of endometrium (ab), 250
Protein synthesis, patterns of, in HeLa cancer cell, 746
Pseudoarthrosis, congenital, of clavicle (ab), 718
Pseudogout, hyperparathyroidism, and carpal-tunnel syndrome: case report (ab), 719
Pseudohypoparathyroidism, familial: role of parathyroid hormone and thyrocalcitonin (ab), 718
Pulmonary carcinoma, its value in determining surgical resectability in: pre and postirradiation azygography, 83
coccidioidomycosis (ab), 474
complications and water retention in prolonged mechanical ventilation (ab), 233
diseases, characterization of shape and location of perfusion defects in certain (ab), 474
edema, acute, in falciparum malaria: clinicopathological correlation (ab), 233
embolism, factors contributing to lowered mortality from (ab), 234
findings, residual, in clinical hyaline-membrane disease (ab), 473
function, regional, changes in, following bronchography (ab), 933
hemosiderosis, idiopathic, in children (ab), 232
lesion, solitary, due to Coccidioides immitis (ab), 474
oxygen toxicity, radiographic features of, in newborn: bronchopulmonary dysplasia (ab), 234
pathology, comparison of findings by angiography and scintigraphy in (ab), 235
Radiation induced neoplasia following external beam therapy for children with retinoblastoma, 529
injury, ultrastructural, development of, 147
interstitial, in management of malignant disease of facial structures, 14
ionizing, effects of, upon immature rabbit larynx, 791
ionizing, tolerance of bed and response of multifocal squamous cell carcinomas to; dystrophic epidermolysis bullosa: report of case, 644
long half-life, and low energy sources, permanent interstitial therapy using, 157
response in relation to cell cycle *in vivo*, 734
therapy and oxygen breathing, changing perspectives in, 665
therapy, cutaneous reactions after; report of 7 cases, 636
therapy, echoencephalography in management of patients receiving (ab), 249
therapy, long time survivals of patients with cancer of eye and surrounding structures treated with, 566
therapy of carcinoma of anterior nasal cavity, 550
therapy of medulloblastoma, twenty years' experience with, 37
therapy, radical, clinical course of Hodgkin's disease and other malignant lymphomas treated with, 618
therapy, response to, of osseous lesions detected on radioisotope bone scans, 137
tolerance of thoracic spinal cord, 659
Radical radiation therapy, clinical course of Hodgkins' disease and other malignant lymphomas treated with, 618
Radioactive isotopes, skin exposure from handling syringes containing, 897
Radioisotope bone scans, response to radiation therapy of osseous lesions detected on, 137
renal function studies in human renal allografts: value in differential diagnosis of oliguria in presence of obstructive disease with and without urinary extravasation (ab), 243
renography in assessment of renal function in newborn (ab), 242
scanning in experimental and clinical orthotopic liver transplantation (ab), 237
Radioisotopic technic, modified, evaluation of peripheral circulation in diabetics by means of (ab), 248
Radiopacity of various ingested foreign bodies in pharynx and esophagus, evaluation of (ab), 713
Radiosensitizer in treatment of neoplasms of head and neck: hydroxyurea, 555

Radiotherapy and intra-arterial infusion, combined, for treatment of advanced cancer of head and neck, 20
definitive, of primary mediastinal seminoma, 86
megavoltage, management of cervical lymph node metastasis by, 74
planning, light analog system for, 648
value of, in management of esophageal cancer, 500
Radium containers, plugging of leaks in, 689
dosage patterns in treatment of uterine carcinoma, 110
therapy, interstitial, clinical application of computer dosimetry in, 165
Reactions, cutaneous, after radiation therapy; report of 7 cases, 636
Rectal dosimetry catheter, new, for use in radiation therapy of carcinoma of uterine cervix, 120
Renal arterial hypertension, excretory urogram in (ab), 242
arteriography and isotope renography in evaluation of renal transplants, 682
disease, polycystic, presenting as medullary sponge kidney (ab), 240
function, radioisotope renography in assessment of, in newborn (ab), 242
function studies, radioisotope, in human renal allografts: value in differential diagnosis of oliguria in presence of obstructive disease with and without urinary extravasation (ab), 243
transplantation, aseptic necrosis following (ab), 935
transplants, evaluation of, isotope renography and renal arteriography in, 682
tuberculosis: role of nephrotomography and angiography (ab), 241
veins, thrombosis, and inferior vena cava complicating lupus nephritis (ab), 477
Renography, isotope, and renal arteriography in evaluation of renal transplants, 682
radioisotope, in assessment of renal function in newborn (ab), 242
Retinoblastoma, radiation induced neoplasia following external beam therapy for children with, 529
Reynolds Historical Library (E), 699
Rhinorrhea, cerebrospinal fluid, studied with gamma scintillation camera (ab), 483
Roentgencinevideography: technique and note on dosimetric problem (ab), 476
Roentgenograms, lateral, localization of calcified pineal body on, 287
plain, of hands, study of inter- and intra-observer error in reading; "to err is human," 853
routine spot, need for: mammographic technique, 880
Roentgenography, three dimensional, 903
Roentgenologic studies of cerebrospinal fluid formation in dog, 756

Sarcoidosis of skull: report of case, 322
Scale, image enlargement, for stereotactic surgery, 270
Scanning, fluorescent thyroid, 721
radioisotope, in experimental and clinical orthotopic liver transplantation (ab), 237
serial brain, with technetium 99m pertechnetate in cerebral infarction, 728
technique, ultrasound, and diagnostic findings; echographic diagnosis of retroperitoneal lymph node enlargement, 438
Scans, radioisotope bone, response to radiation therapy of osseous lesions detected on, 137
Schistosomiasis of spinal cord, 400
Scintigraphy and angiography, comparison of findings by, in pulmonary pathology (ab), 235
with ^{203}Hg and ^{99m}Tc in diagnosis of brain tumors (ab), 473
Seat belt fractures: report of two cases (ab), 244
injuries (ab), 934
Seminoma, primary mediastinal, definitive radiotherapy of, 86
Siredon mexicanum, adult, effects of partial irradiation on tail regeneration in, 196
Singleton, Arthur C., M.D., 1900–1968 (E), 210
SJL/J mouse Hodgkin's-like reticulum cell sarcoma, extended vs. local fields in radiocurability of; basis for segmental sequential irradiation in Hodgkin's disease, 806
Skin exposure from handling syringes containing radioactive isotopes, 897
Skull, base of, cartilaginous tumors of, 308
cloverleaf (ab), 473
sarcoidosis of; report of case, 322
Small intestinal epithelium of dogs, enhancement of x-ray effects on, by Actinomycin D, 126
Smith-Lemli-Opitz syndrome: case report (ab), 712
Sodium diatrizoate, hypaque, injection of, in management of abdominal stab wounds (ab), 476
Spinal cord, schistosomiasis of, 400
cord, thoracic, radiation tolerance of, 659
hemorrhage, epidural, spontaneous, 383
Spine, cervical, neurologic complications of Paget's disease in, 375
Spleen, spontaneous rupture of, in plasma cell leukemia (ab), 716
Spondylolysis, acquired, in child and young adult: report of two cases (ab), 719
cervical, roentgenographic correlations in, 370
Squamous cell carcinomas, multifocal, tolerance of bed and response of, to ionizing radiation; dystrophic epidermolysis bullosa: report of case, 644

Stereotactic surgery, image enlargement scale for, 270
precise alignment of x-ray beams for, 260
Stockholm applicator, simple modification of, for treatment of early cancer of uterine cervix, 115
Subarachnoid cysts, suprasellar; radioclinical features, 291
Subdural hematomas, ultrasonic diagnosis of, 413
Supracondylar process and its fracture, 844
Syndrome, carpal-tunnel, pseudogout, and hyperparathyroidism: case report (ab), 719
Goldenhar's (oculoauriculovertebral dysplasia), roentgenologic aspects of (ab), 230
iatrogenic afferent-loop (ab), 934
Smith-Lemli-Opitz: case report (ab), 712
Syringes containing radioactive isotopes, skin exposure from handling, 897

Table, simple biplane myelographic, 411
Tail regeneration, effects of partial irradiation on, in adult Siredon mexicanum, 196
Technetium 99m pertechnetate, serial brain scanning with, in cerebral infarction, 728
Telecobalt split field dosimetry; with special reference to central penumbral isodose separation, 152
Temporal artery, superficial, aneurysms of, 331
bone in Paget's disease, tomography of, 838
Tentorial hiatus, vascular malformations of posterior fossa including, 341
Tetralogy of Fallot, angiographic and catheterization findings in patients with difficulties after total correction of (ab), 235
Thermography in occlusive cerebrovascular disease (ab), 231
Third ventricular catheterization, selective, for pantopaque ventriculography, 348
Thoracic esophagus, cancer of, surgical and radiation treatment of, 523
spinal cord, radiation tolerance of, 659
Thrombi, arterial and venous, experimental study of recanalization of (ab), 481
Thyrocalcitonin and parathyroid hormone, role of: familial pseudohypoparathyroidism (ab), 718
Thyroid scanning, fluorescent, 721
Tomography of temporal bone in Paget's disease, 838
Tongue, cancer of base of; 116 patients treated radiotherapeutically in 11 year period 1952 through 1962, 26
Transfusion, exchange, colonic perforation after (ab), 716
perforation of bowel in newborn as complication of (ab), 715
spontaneous perforation of bowel in newborn following (ab), 476
Transplantation, renal, aseptic necrosis following (ab), 935
Transplants, renal, evaluation of, isotope renography and renal arteriography in, 682
Tuberculosis, renal: role of nephrotomography and angiography (ab), 241
Tumor, Wilms', angiographic manifestations of; observation of six cases, 95
single *versus* multiple dose dactinomycin therapy of (ab), 249
Tumors, brain, scintigraphy with ^{203}Hg and ^{99m}Tc in diagnosis of (ab), 473
cartilaginous, of base of skull, 308
of nasopharynx, influence of relationship "local tumor extent-time" upon evolution of, 536
pituitary, stereotaxic transsphenoidal biopsy and cryosurgery of, 273
solid, surgical management of, in childhood, 105
smooth-muscle, of esophagus (ab), 236

Ultrasonic diagnosis of subdural hematomas, 413
Ultrasonography, modified technique of, for detection and differential diagnosis of breast lesions, 446
Ultrasound exploration, B-scan, of neoplastic disease, 428
scanning technique and diagnostic findings; echographic diagnosis of retroperitoneal lymph node enlargement, 438
Ureteral injuries recognized after gynecologic operations (ab), 477
reflux in adults (ab), 935
Urethral resistance and shape in girls, correlation of (ab), 936
Urethrocystography (ab), 243
Urogram, excretory, in renal arterial hypertension (ab), 242
Urography, intravenous, extravasates with (ab), 241
Uterine carcinoma, radium dosage patterns in treatment of, 110
cervix, carcinoma of, new rectal dosimetry catheter for use in radiation therapy of, 120
cervix, early cancer of, simple modification of Stockholm applicator for treatment of, 115
Uterus, adenocarcinoma of, 603

Vascular malformation of posterior fossa including tentorial hiatus, 341
Ventilation, mechanical, prolonged, pulmonary complications and water retention in (ab), 233
Ventriculography, pantopaque, selective third ventricular catheterization for, 348
Vitallium mold arthroplasty of hip, roentgenologic

and clinical evaluation of (ab), 481
Vitamin B_{12} malabsorption, mechanism of, in patients receiving colchicine (ab), 237

W. Walter Wasson, M.D., 1884–1968 (E), 456
Water-soluble radiopaque media, brain barrier to: effect of parabens on permeability of blood, 404
Wigby, Palmer E., M.D., 1903–1968 (E), 921
Wilms' tumor, angiographic manifestations of; observation of six cases, 95
single versus multiple dose dactinomycin therapy of (ab), 249
Wrists, triangular cartilage calcification in; its incidence in elderly persons, 850

X-ray beams, precise alignment of, for stereotactic surgery, 260
effects, enhancement of, on small intestinal epithelium of dogs by Actinomycin D, 126
fluorescent screen-film systems, line spread-function and modulation transfer function of, —problems with double-coated films, 909

AUTHOR INDEX TO VOLUME 105

*=Original Article

Abou-Khatwa, Hassan, 248
Adams, Donald, *273
Agarwal, K. N., *319
Alders, M. A., *147
Allen, E. H., 244
Allen, Samuel D., 482
Amplatz, Kurt, *682, *784
Apostolopoulou, E., 232
Aral, Isamettin, *110
Aron, Bernard S., *37
Ashburn, William L., *483
Asher, W. Michael, *438
Aufrance, Otto E., 481

Babbitt, Donald P., *352
Badib, Ahmed O., *596
Bagshaw, M. A., *74
Bagshaw, Malcolm A., *86
Baltaxe, Harold A., *784
Bandtlow, K., 243
Barry, Kevin G., 233
Bateson, E. M., 243
Batsakis, John G., 475, 717
Batson, Hugh M., 243
Baum, Sheldon, *137
Becker, Joshua A., 241
Beitia, Antonio A., *596
Beland, J. E., 474
Bender, R., 230
Bennett, L., 933
Bergland, Richard M., *756
Berk, R., *352
Berkman, Milton, 230
Berkmen, Yahya M., *298
Bertino, Joseph R., 484
Bhandari, Y. P., *386
Bhardwaj, O. P., *319
Bickel, William H., 718
Binnington, V. I., 473
Birchall, Robert, 243
Bland, John H., *853
Blennerhassett, John, 935
Bloom, H. J. G., *43
Bohatirchuk, F., 478
Bohorquez, J. F., *536
Bonfield, Robert E., 475
Bonfiglio, Michael, 478
Bonte, Frederick J., *791
Boström, H., 245
Boyer, Carl W., Jr., *14
Brettschneider, Lawrence, 237
Brickner, Theodore J., Jr., *14
Brieden, M., *897
Brijs, A., 241
Briner, William H., 483
Broadwater, John R., *609
Brooks, Marion H., 233
Brooks, V., 243
Broussin, J., 247
Brown, B. St. J., 713
Brown, Donald W., 237
Brown, Estelle, *853
Brown, Robert A., *860
Brucher, Jack, *298
Brun, J., 235
Brunst, V. V., *196
Bruwer, André J., *390
Bryan, Charles S., 715
Buchwald, Henry, *784
Burge, Curtis H., 921
Burhenne, H. Joachim, 934
Burko, Henry, 473
Burn, J. Ian, 245
Buschke, Franz, *659
Buschke, Franz J., *614
Byrne, R. N., *880

Campbell, Crawford J., 478
Campbell, D. R., 713
Carroll, T. B., 244
Carruthers, R. H., 935
Carter, Peter R., *142
Cassady, J. Robert, *529
Castor, W. R., 476
Castro, Joseph R., *165
Castro, Leonidas, *7
Chait, Arnold, *400
Chamberlain, George E., 474
Chambers, Robert G., *555
Chang, Pauline K., 484
Chapdelaine, Alcide, *291
Chase, Norman, *413
Chiche, P., 246
Chodos, Robert B., 237
Clay, Lavern, *115
Clayton, R. S., *897
Clayton, Ruth V., *853
Cleaveland, James D., 237
Clouse, Melvin E., 481
Cohn, Isidore, Jr., 937
Cole, Christine, *126
Coleman, William P., *636
Colwell, Edward J., 714
Concannon, Joseph P., *126
Cooke, Allan R., 934
Cooley, Denton A., 933
Cordes, David J., 237
Corkery, J. J., 716
Cornell, Steven H., 235
Cosbie, W. G., *487
Costopoulos, L. B., 239
Crestin, M., 239
Crue, Benjamin L., Jr., *270
Cruess, Richard L., 935
Curry, Joseph L., *894

Damascelli, Bruno, *428
Danahy, Daniel T., *404
D'Angio, G. J., 249
Darke, Christopher S., 714
Darling, D. B., 230
Dashe, Alfred, *273
Davenport, James H., *137
Davidson, Harold D., *682
Davidson, J. W., *763, 936
De Albertis, P., 476
Declercq, A., 479
DeLand, Frank H., *446
de la Pava, Samuel, *7
Delclos, Luis, *603
Dellenbach, P., 240
del Regato, J. A., 208
Dent, C. E., 478
d'Escrivan, Julio C., 482
Deverall, P. B., 236
Devine, Kenneth D., *26
Dextroux, J., 479
di Chiro, Giovanni, 483
Dick, Harold M., 719
Digel, Joseph, *518
Dobbs, J., *352
Dodds, Wylie J., *850
Dodinval, P., 479
Dossetor, John, 935
Dotter, Charles T., 246
Dubowitz, V., 716
Duplantis, Fernand, *291
duV Tapley, Norah, *172

Eades, Sheila M., 715
Earle, John D., *86
Edgren, B., 245
Edland, Robert W., *644
Ehrenhaft, Johann L., 235
Eisenberg, Eugene, 480
El Gammal, T., *830
Elkin, Milton, *95
Elliott, John, 242
Ellsworth, Robert M., *529
Engelbrecht, H. E., 478
Eyring, Edward J., 480

Fabrikant, Jacob I., *734
Faloon, William W., 237
Fannin, T. F., 718

Fays, J., 239
Feder, Bernard H., *157
Feingold, Murray, 230
Feldman, Frieda, *375
Ferris, E. J., *370
Figueroa, Julio E., 243
Fisher, Bernard, 937
Flanc, Charles, 481
Fletcher, Gilbert H., *165, *172, *603
Fonts, E. A., *120
Forsberg, Leigh, 240
Fossati, Franca, *428
Fox, James E., 717
Frantz, Andrew G., 718
Fraser, F. C., 484
Freedman, Gerald S., *648
Freimanis, Atis K., *438, 454
Friedenberg, Z. B., 244
Friedmann, G., 712

Gabrielsen, Trygve O., *361
Galasko, C. S. B., 245
Galluzzi, S., 475
Gannon, William E., *400
Garcia-Bengochea, Francisco, *260
Garciga, C. E., *147
Garrison, J. B., *903
Germain, J. P., 477
Gershon-Cohen, J., *880
Gertner, Harold R., Jr., 476
Gilladoga, Angela, *777
Gillot, C., 246
Glenn, Frank, 716
Godfrey, R. C., 478
Goepfert, Helmuth, *20
Goldberg, Barry B., 249
Goldenberg, David B., *518
Goldstein, Arthur G., 482
Gondos, Bela, 248
Goodner, John T., *523
Goodwin, Paul N., *648
Gopala Rao, U. V., *518
Goulston, Kerry, 934
Grabow, Jack D., 231
Grace, Donald, 242
Grainger, Ronald G., 932
Grant, D. G., *903
Grantham, S. Ashby, 719
Green, Allan E., Jr., *609
Greenbaum, Edward I., *885
Gregor, W. M., 713
Gronner, Arthur T., *365
Gros, Ch., 240
Grossman, Herman, *777
Groth, Carl G., 237
Gruber, F. H., 244
Gruber, Frank H., *305
Guier, W. H., *903
Gunn, Walter G., *157
Gupta, S. K., *386
Gutierrez, Augusto G., *603

Habeck, Edgar A., 483
Hahar, Constance Q., 237
Hall, M. R., 210
Hallman, Grady L., 933
Haluska, G., *814
Haluska, Glenn, *806
Hamilton, J. R., 934
Hamilton, Carlos R., Jr., 477
Hammon, William M., *326
Hancock, James A., Jr., *609
Hanks, G. E., *74
Harbert, John C., 483
Harris, Martin E., *383
Harrow, Benedict R., 477
Hassaballa, Abdel Monem, 248
Hassim, Abu M., 935
Hellman, Samuel, *618
Hendee, W. R., *147
Henderson, J. A. M., 474
Henk, J. M., *43
Hermel, M. B., *880
Hers, J. F. P., 933
Heully, F., 239
Heuser, Gunnar, *273
Hodges, Paul C., *260
Hoffer, Paul B., *721
Holt, John F., *314
Howie, P. W., 236
Howes, J. M., 474
Hudson, J. D., *334
Hudson, Page, 716
Hynes, David M., 932
Hynes, John F., *629

Isard, Harold J., 249

Jeletzky, T., 478
Jesse, Richard H., *20
Johner, Carl H., 482
Johns, David G., 484
Johns, R. J., *903
Johnson, K. G., 484
Johnson, Robert H., *20
Johnson, T. H., Jr., *890
Johnston, G. S., 936
Johnston, Richard B., Jr., 473
Joynt, Robert J., *334
Judkins, Melvin P., 246

Kahn, Paul C., *772
Kaplan, H. S., *74
Karpouzas, J., 232
Kattan, Kenneth R., 240
Keats, Theodore E., *314, *830
Kellerhouse, L. E., *877
Kennedy, B. J., 250
Kiel, Frank W., 233
Kier, E. Leon, *341
King, John, *126
Kitchen, R. E., *411
Klatte, Eugene C., 473
Kligerman, Morton M., *618
Klotz, P. G., 935
Kohanim, M., 244
Kolodny, Gerald M., *746
Kricheff, Irvin, *413
Krivit, W., 249
Kroening, Paul M., *900
Kurohara, Samuel S., *115, *596

Lame, Edwin L., *359
Lamoureux, Christian, *291
Lattimer, John K., 241
Laurent, Y., 479
Laver, Myron B., 233
Leblanc, Pierre, *291
Lebouchard, R., 246
Lebrun, J., 479
Ledoux, Roger, *291
Lee, James B., 718
Legters, Llewellyn J., 714
Le May, M. L., *370
Leone, Anthony J., Jr., 715
Leucutia, Traian, 699
Levin, Aaron R., *777
Levitus, Z., 717
Lewin, W., 932
Lewtas, Norman A., 714
Li, J., 245
Lindberg, Robert D., *20, *165
Lister, James, 716
Little, J. M., 234
Livraghi, Tito, *428
Loewenthall, John, 234
Loken, Merle K., *682
Lorber, John, 712
Lorch, Gerald S., *772
Lott, Stewart, *518
Lubberts, G., *909
Lubin, E., 717
Lucas, Cynthia, 935
Lucke, H. H., 713
Lupu, Andrei N., 242

McBean, James B., *26
McLaughlin, William T., *86
McSherry, Charles K., 716
Macdonald, F. Robert, 935
Mack, Pauline Beery, *870
Maclean, Lloyd D., 935
Maier, John G., *14
Manchester, J. S., 713
Mankiewicz, E., 474
Marcial, Victor A., *586
Martel, William, 475
Martin, Charles L., *566

Martin, Lester W., *105
Martin, P. L., 247
Mason, E. W., *689
Matsaniotis, N., 232
Mawdsley, C., 231
Maxfield, William S., 243, *636
Maxwell, Morton H., 242
Meharg, Louis S., *870
Mendoza, R. Diaz, *514
Meng, Chien-Hsing, *95
Merli, E., 476
Messaritakis, J., 232
Meyniel, G., 235
Millard, F. J. C., 244
Miller, George, *806
Miller, J. D., 236
Minagi, Hideyo, *308, *365
Molina, C., 235
Moosa, A., 716
Morisaki, Naoki, 719
Mould, Richard F., *152
Mucha, Raymond, *900

Nassim, J. R., 244
Nathan, Fred F., 718
Neal, M. P., Jr., *411
Nemoy, Norman J., 240
Newman, Alex, *844
Newton, Thomas H., *308
Newton, W. A., Jr., 249
Nicolesco, N., 232
Nilsonne, U., 245
Northway, William H., Jr., 234

O'Brien, Mark S., *341
O'Loughlin, B. J., *885
Ooi, Yoshio, 719
O'Reilly, R., 933
O'Reilly, Richard J., *404
Orme, R. L'E., 715
Owano, Luis R., 717

Pace, William G., 715
Pagano, C., 476
Papademetriou, Theodore, 478
Paquot, J. P., 479
Park, C. H., *795
Partington, M. W., 473
Pawl, Ronald P., *287
Payne, R. F., 238
Pearson, J. G., *500
Penny, Stuart F., 474
Perry, Ronald H., *14
Petasnick, Jerry P., *838
Peters, Leo M., 483
Phillips, Theodore L., *659
Pittman, H. H., *795
Plagne, R., 235
Podolak, G., *885
Pontoppidan, Henning, 233
Pool, John L., *3
Porrath, Saar, *63
Potts, D. Gordon, *756
Poulose, Kattadiyil, 474
Poulter, C. A., *814
Poulter, Colin A., *665
Prevot, H., Jr., 473
Pribram, H. F. W., *334, *411
Proctor, Robert F., 714
Prosnitz, Leonard R., *618

Quick, Raymond S., *665
Quinn, James L., III, *728
Quinn, James Leland, III, *251

Radcliffe, W. B., *795
Rand, Robert W., *273
Ranniger, K., *877
Ranniger, Klaus, 482
Razzak, Muhammad Abdel, 248
Reagan, T. A., *890
Reba, Richard C., 474
Redick, Thomas J., *359
Reef, James D., *791
Reichert, Albert, 712
Reid, M. McC., 718
Reilly, B. J., 717
Renouf, J. H. P., 936
Richards, George J., Jr., *555
Rider, W. D., *514
Rinker, Carl T., *83
Rivers, Robert J., Jr., *404
Robert, F. W., 246
Robertson, Alex, 242
Robichon, J., 477
Rodriguez, A., *897
Rogoff, Stanley M., 919
Rogow, Edward, *126
Rosan, Robert C., 234
Rösch, Josef, 246
Rosillon, J., 479
Roth, Nathan, *273
Rothman, Jeffrey, *413
Rozenfeld, M. L., *689
Rubin, P., *814
Rubin, Philip, *665, *806
Rusiewicz, E., 717
Rutledge, Felix N., *603
Ruvalcaba, R. H. A., 712
Rybak, James J., 715

Sagerman, Robert H., *529
Saha, M. M., *319
Salmon, James H., *298
Samuel, E., 231
Sansregret, André, *291
Sato, K., 484
Scallon, Joseph E., *157
Scanlon, Paul W., *26
Scatliff, J. H., *795
Schechter, Mannie M., *341
Schneider, C., 473
Schober, R., 230
Schubert, Edward T., *777
Schwarz, George, *579
Scott, Wendell G., 456
Seaman, William B., *375
Sellwood, R. A., 245
Severini, Aldo, *428
Shatsky, Stanley, *413
Sheehy, Thomas W., 233
Sheers, Geoffrey, 234
Sheldon, J. J., *120
Shepard, Frank M., 473
Shimeoni, A., 717
Silver, Lawrence, *137
Sklaroff, David M., 249
Slack, Nelson, H., 937
Sladen, Arnold, 233
Smith, David W., 712
Smithwick, Walter, III, 476
Snyder, Samuel L., *157
Son, Yung H., 247
Sondhaus, Charles A., *157
Soter, Constantine S., 715
Soule, A. Bradley, *853
Soule, Edward H., *26
Spencer, Richard P., 484
Spira, Jacob, *110
Spitz, Harold B., 240
Stahlman, Mildred, *473
Starzl, Thomas E., 237
Steinbach, Howard L., *850, *860
Stembridge, Vernie L., *791
Stephens, P. J. T., 716
Storey, G. O., 480
Strain, William H., *404
Streets, James M., 718
Strickland, Basil, 720
Stubenbord, William T., 716
Sugawara, Sachiko, 719
Sumerling, M. D., 231
Summers, Roy E., *126
Suprenant, E., 933
Suzuki, Yajuro, 719

Tang, T., *352
Tashjian, Armen H., Jr., 718
Tcherkow, George, *126
Templeton, Ann R., 234
Templeton, Arch W., *83
Thomas, Martin R., *404
Thomford, Neil R., 715
Thorslund, T. W., 484
Tismer, R., 712
Todd, Edwin M., *270
Tomé, José M., *586
Tréheux, A., 239
Tretter, Patricia, *529
Tubiana, M., *178

Tumulty, Philip A., 477
Turano, L., 479
Turner, F. W., 239
Turner, Oscar A., *322
Tzonos, T., 473

Ubiñas, Jeannie, *586
Uchida, Suguru, *185
Usher, Michael S., *728

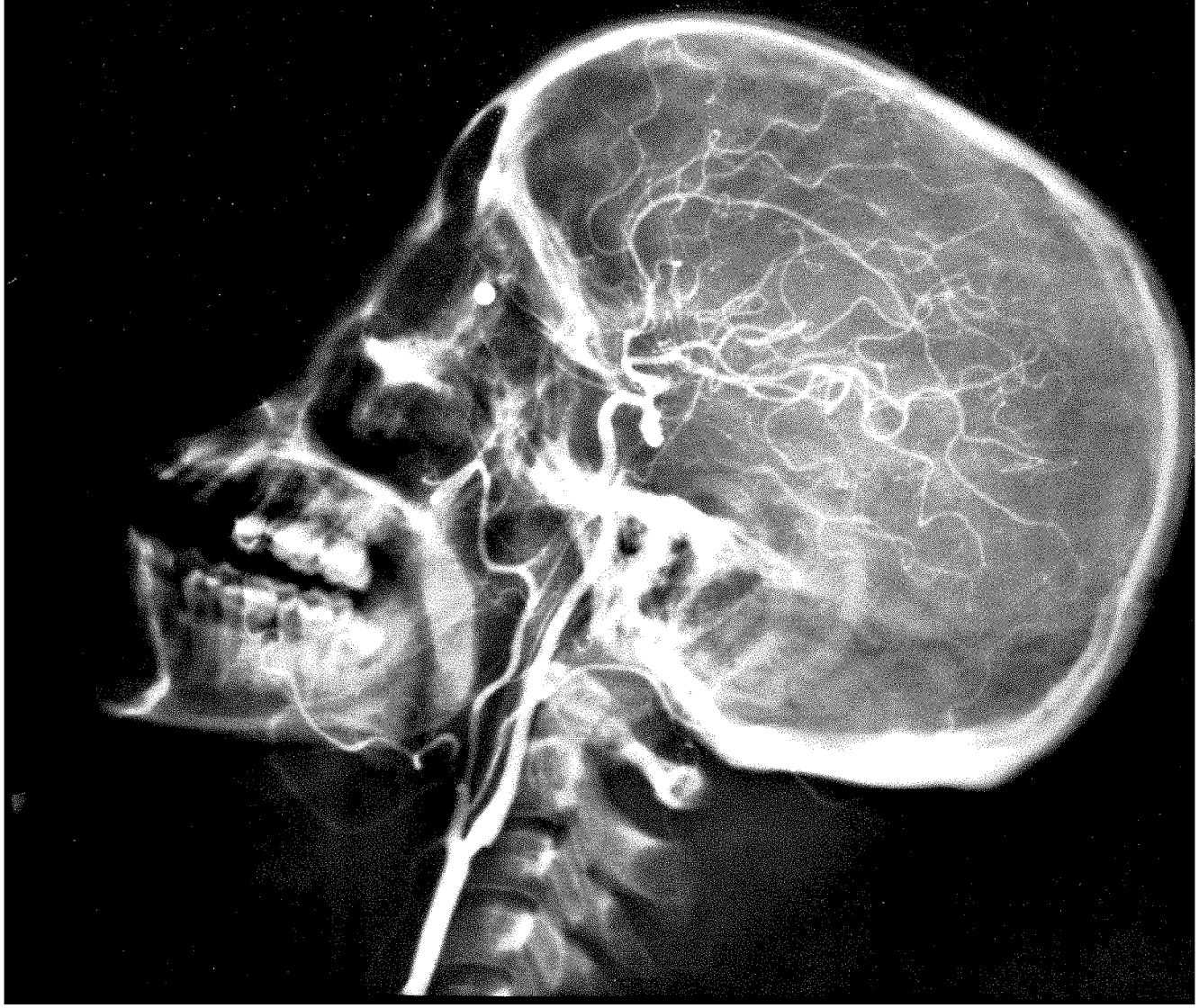
Vaeth, Jerome M., *614
vanBuskirk, Frederick W., *853
Varco, Richard L., *784
Viallet, J. F., 235
Viallet, P., 235
Vignolini, R., 476
Vlad, Peter, 235
Vogt, Fred B., *870
Von Essen, Carl F., *618
Von Ronnen, J. R., 482
Vuksanovic, M., *120

Wagner, Henry N., Jr., 474
Wallace, E. N. K., *43
Walter, Arthur K., *287
Walter, J. P., 240
Wanebo, C. K., 484
Webb, Dale I., 237
Webber, M., 933
Weber, Alfred L., 481
Webster, John H., *7, *596
Weinstein, Joel D., 719
Weiss, Robert M., 241
Weiss, Sanford R., *322
Welsh, Jack D., 714
Wester, P. O., 245
Westerman, B., 245
Wetzel, Richard A., 247
Whitaker, J., 936
Whitcomb, Wayne P., *550
White, J. E., *897
Wilkinson, H. A., *370
Wilkinson, Harold A., *348
Wilson, A., 933
Wilson, Charles B., *331
Wilson, Robert M., *404
Wilson, William J., 247
Winchester, Patricia, *777
Winter, Chester C., 242
Wold, G. J., *120
Wolfel, Donald A., *142
Wolff, J. A., 249
Wollin, D. G., 473

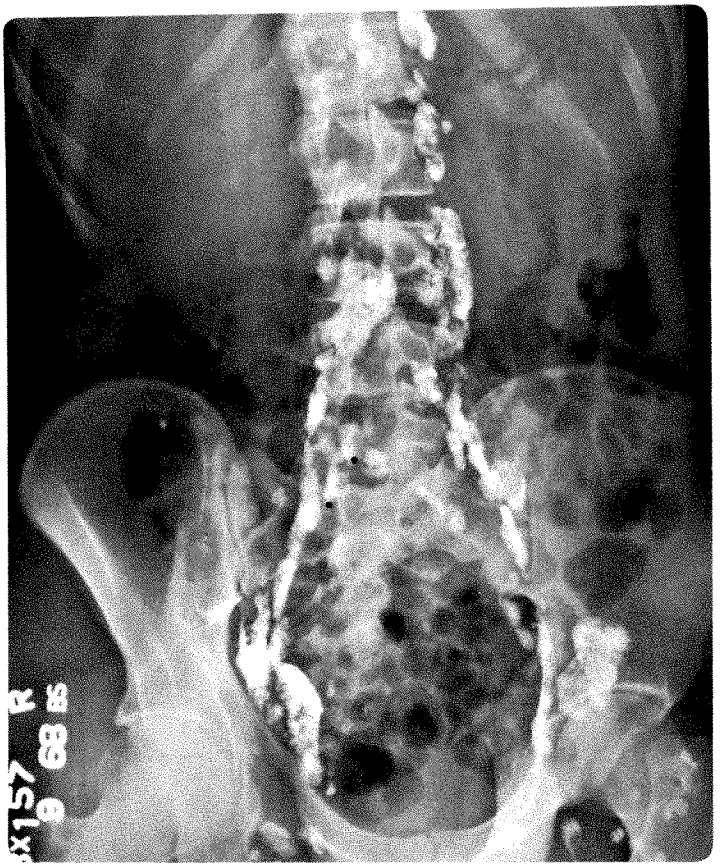
Yamazaki, Norio, 719
Young, G. B., 231
Young, Irving S., *390

Zachary, R. B., 712
Zarghami, Gholam H., *115
Zeppieri, Joseph P., *772
Zingesser, Lawrence H., *341
Zittel, R. X., 473
Zucconi, A., 476
Zuidema, George D., 476

90 second proof







KODAK *RP/S* X-OMAT Medical X-ray Film—significantly faster for minimum exposure.



KODAK *RP/L* X-OMAT Me
X-ray Film—records the
range of tissue densities.

KODAK *RP* X-OMAT Films give more information, time after time.

Quality is the heart of the Kodak 90-Second System. And that's precisely why it gives you more information, film after film.

In Kodak terms, quality includes film choice. You choose which of the three 90-second films best meets your requirements for more of the information you're after.

Superior processing is the rest of the Kodak quality story. It's a short story: 90 seconds from exposed film to clear readability.

Credit goes to the KODAK *RP* X-OMAT Processor and the new low-temperature, long-life chemicals. The outcome: more information in your radiographs.

For quality results in 90 seconds, take the steps you know will lead directly there—with KODAK *RP* X-OMAT products.

Kodak

EASTMAN KODAK COMP



As Ever,

We would have (if we could have) changed it to make it better—never just to make it different. But little in the past century of medical progress has suggested a compound superior to Phospho®-Soda for gentle, predictable laxative action. Rely on it for freedom from urgency, griping, irritation, or nausea. For use in almost any age group. Available regular or flavored.
Warning: Do not use when nausea, vomiting or abdominal pain is present. Frequent or prolonged use of this preparation may result in dependence on laxatives.

Phospho®-Soda

Buffered Laxative

1869-1969

Fleet® pharmaceuticals

A century of service to medicine



F38A69

C. B. FLEET CO., INC., Lynchburg, Va. 24505



Picker's new automatic chest x-ray system...

doubles capacity for chest examinations and frees general purpose equipment for other patients.

The new Picker system is automated. It can handle twice as many chest x-rays per unit of time. The general purpose equipment which you now use for chest examinations (typically almost half of all examinations) can be made available for other work.

Accordingly, installation of this new Picker chest x-ray system can virtually double the capacity of a radiology department. The effectiveness and convenience of this automated system is related to several new developments. For example...

The x-ray tube and exposure chamber—moving together in servo-synchronized alignment—simplify and accelerate patient positioning.

Uses large capacity, light-tight, cutfilm magazines which hold up to 125 sheets of 14″ x 17″ noninterleaved film just as it comes from the box.

Excellent radiographic detail is achieved by vacuum-enforced film/screen contact at the exposure plane.

The automatic film transport system moves the film from the loading magazine to the exposure chamber and then into the receiving magazine in just 3 seconds.

And finally: the insertion of the patient's ID card in the chest unit photographically imprints his identification on his radiograph.

To learn more about how our new system can double your capacity, see your local Picker representative. Or write to Picker X-Ray, 595 Miner Road, Cleveland, Ohio 44143.

PICKER

Timely Technetium.

NEISLER now ships NEIMOTEC® Sterile Generators ($^{99}Mo/^{99m}Tc$) 156 days a year to simplify your scanning scheduling.

We ship technetium 99m generators every Wednesday, every Friday, and every Sunday* so that your diagnostic needs, whatever they are today, or might become tomorrow, are likely to be met with minimum trauma. Simply tell us how many millicuries of technetium 99m you need on Monday, Tuesday, Wednesday, Thursday, Friday, Saturday and even on Sunday, and we will show you how our three-day-a-week NEIMOTEC® generator shipments can best meet your specific requirements economically.

About the Generator—This is a complete system which is easy to set-up and use. And the unique accessibility of its components allows for adjustments if required. This generator is sterile, pyrogen-free and provides routinely high yields.

Safety Considerations—The NEIMOTEC® generator itself has a well-engineered, effective shield. The eluate vial is married to its own separate lead shield and cannot accidentally leave it.

New Radiometric Assay Kit—This is a complete kit for rapid, accurate and reproducible assay and calibration of the *total* generator eluate. It determines total ^{99m}Tc and ^{99}Mo activities radiometrically in a matter of minutes *without* transferring portions of the eluate from its vial. And no spot tests!

NEISLER Service—(1) Because we are also major suppliers of sodium pertechnetate Tc 99m solution, now calibrated to 3 P.M. New York time, we can always backstop you if required for any reason whatsoever. (2) Local NEISLER salesmen and specialists provide personalized service in virtually all areas. (3) Our Order Department is as near as your phone—call collect—



(212) 682-5057 or 5058. (4) Our Radiopharmaceutical Customer Service Manager (phone 212-682-5057) is available for answering questions or providing technical service having to do with any of NEISLER's radiopharmaceuticals.

Indications—Brain scanning.

Contraindications—Should not be administered to pregnant or lactating women, or to patients under the age of 18 years, except when necessary diagnostic information cannot be obtained by other types of studies or can only be obtained at a risk greater than the radiation exposure caused by this drug.

Warnings—As with all radiopharmaceuticals, dose should be limited to smallest reasonable amount consistent with greatest value in terms of relevant diagnostic information.

Precautions—Approved radiation safety precautions should be maintained at all times. Interpretation of scans should take into consideration the possibility of extracranial contamination with salivary secretions, and should distinguish between abnormalities and areas of normally high vascular activity.

Adverse Reactions—None reported to date; however, patients should be carefully observed.

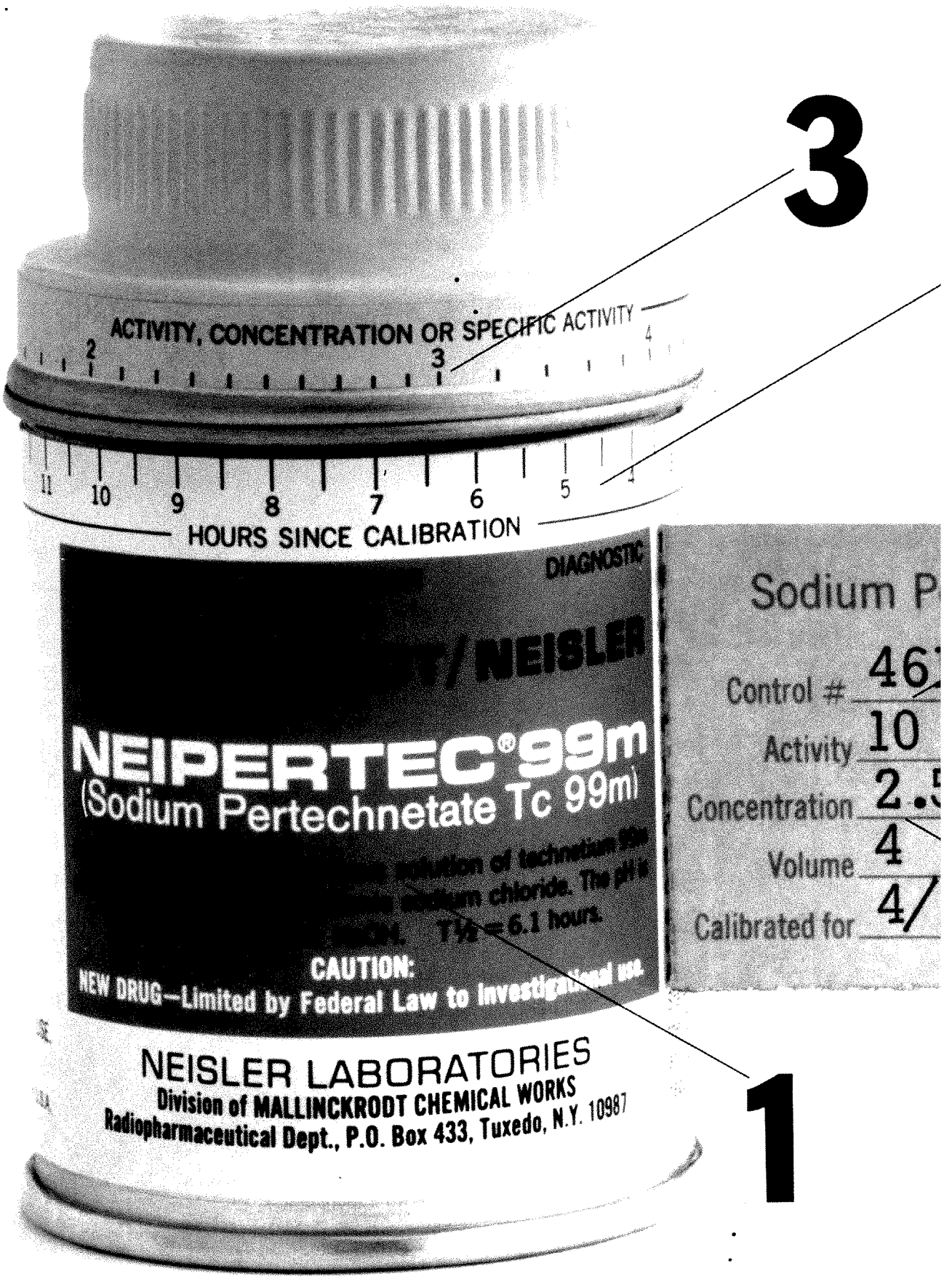
Dosage and Administration—Up to 10 millicuries per patient, administered by intravenous injection. Physicians should consult product package insert before administering.

*Generators shipped on Sunday can be reliably delivered early Monday A.M. in areas serviced by airports having dependable delivery service.

NEISLER LABORATORIES
Division of MALLINCKRODT CHEMICAL WORKS
Radiopharmaceutical Department
P.O. Box 433, Tuxedo, N.Y. 10987 (Phone 212-682-5057)

NEISLER



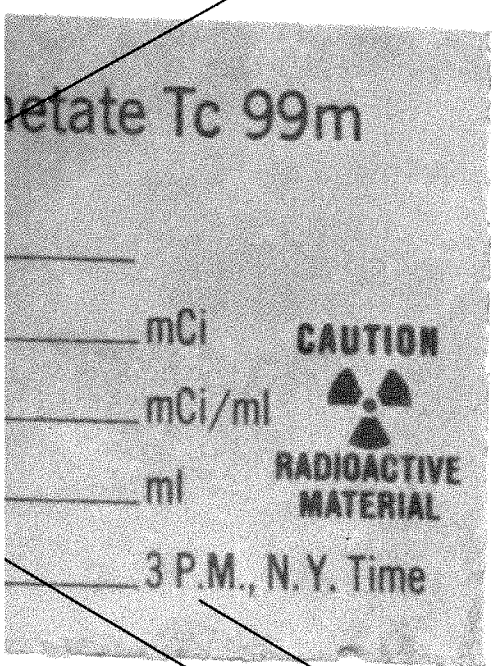

ACTIVITY, CONCENTRATION OR SPECIFIC ACTIVITY
2
3
4
11
10
9
8
7
6
5
4
HOURS SINCE CALIBRATION
DIAGNOSTIC
NEISLER
NEIPERTEC®99m
(Sodium Pertechnetate Tc 99m)
T½ = 6.1 hours.
CAUTION:
NEW DRUG—Limited by Federal Law to investigational use.
NEISLER LABORATORIES
Division of MALLINCKRODT CHEMICAL WORKS
Radiopharmaceutical Dept., P.O. Box 433, Tuxedo, N.Y. 10987
Sodium P
Control # 46
Activity 10
Concentration 2.5
Volume 4
Calibrated for 4/
3
1

The simple route to pure pertechnetate.

(A self-guided tour.)

2

4



5

6

Complete this tour of NEISLER's NEIPERTEC® 99m (sodium pertechnetate Tc 99m). It's the easy route to pure pertechnetate.

1 NEIPERTEC 99m is pure, chemically-processed, free from elution contaminants. Sterile, pyrogen-free.

2 Supplied in a vial locked into a lead shield by a safety ring.

3 The COMPUTERCAP® package allows easy calculation of total activity and concentration at any time.

4 Choice of activities in individual vials: 5, 10 and 15 mCi.

5 Constant concentration: 2.5 mCi per ml. at calibration time.

6 Calibration time is now 3 PM New York time. Delivery 5 days a week, every Monday through Friday.

Any questions? Any problems? Any unusual requirements? There are NEISLER salesmen or specialists in virtually all areas. And our Radiopharmaceutical Customer Service Manager (phone 212-682-5057 or 212-682-5058) can provide technical service on any NEISLER radiopharmaceutical.

Indications—Brain scanning.

Warning—Should not be administered to pregnant or lactating women, or to patients under the age of 18 years, except when necessary diagnostic information cannot be obtained by other types of studies or can only be obtained at a risk greater than the radiation exposure caused by this drug.

As with all radiopharmaceuticals, dose should be limited to smallest reasonable amount consistent with greatest value in terms of relevant diagnostic information.

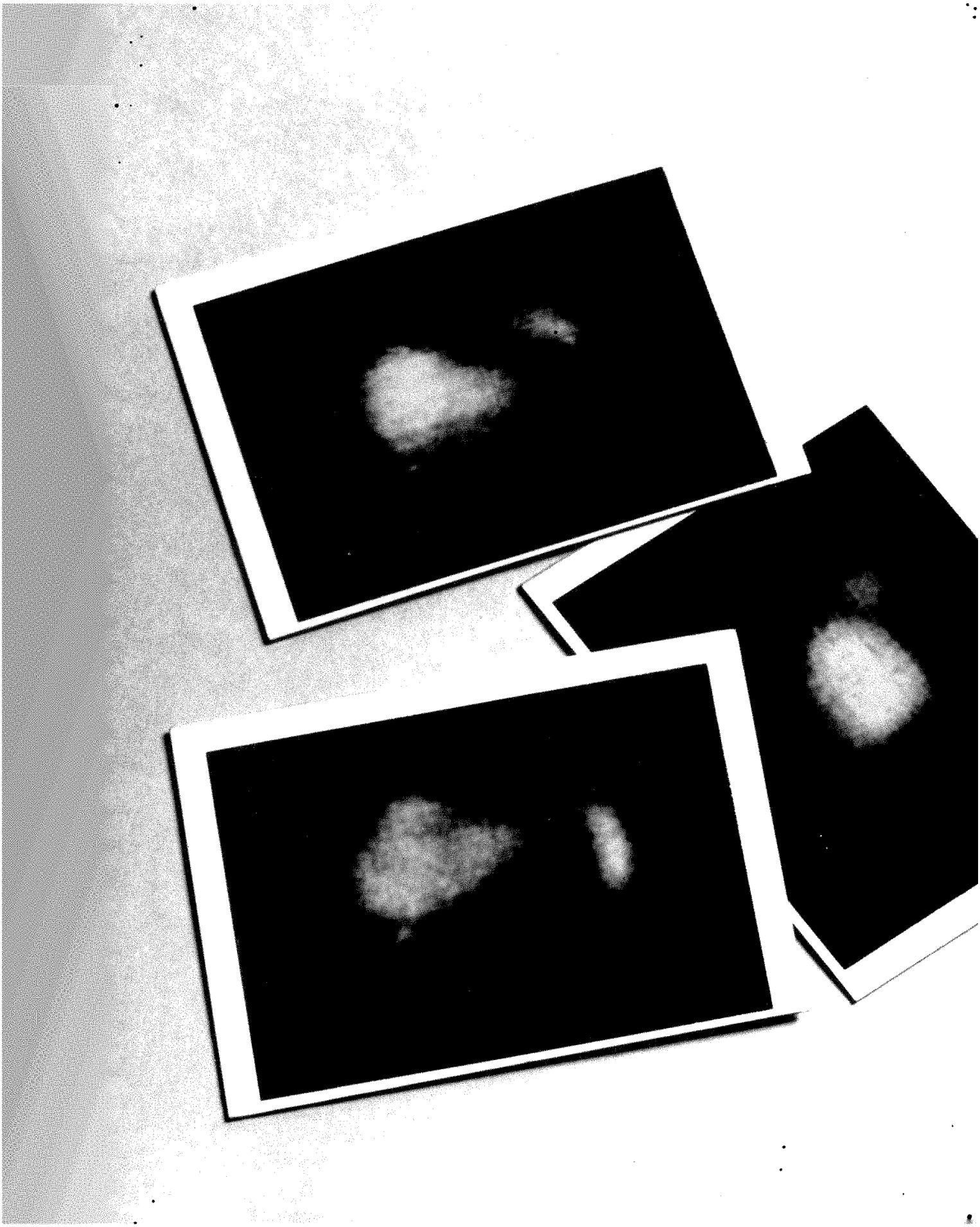
Precautions—Approved radiation safety precautions should be maintained at all times. Interpretation of scans should take into consideration the possibility of extracranial contamination with salivary secretions, and should distinguish between abnormalities and areas of normally high vascular activity.

Adverse Reactions—None reported to date; however, patients should be carefully observed.

Dosage and Administration—Up to 10 millicuries per patient, administered by intravenous injection.

NEISLER LABORATORIES
Division of MALLINCKRODT CHEMICAL WORKS
Radiopharmaceutical Department
P.O. Box 433, Tuxedo, New York 10987
(Phone 212-682-5057 or 212-682-5058)

NEISLER



The technetium that shows you the reticuloendothelial system.

What is it?
Technetium sulfide Tc 99m colloid. A sterile, pyrogen-free, gelatin-stabilized aqueous solution for IV administration.

What is it used for?
Colloidal technetium sulfide is a most useful scanning agent for visualizing liver, spleen, and bone marrow. Such visualization of the liver has been effective in helping to determine size, configuration, location, the presence of space-occupying lesions, and in providing an index of the relative reticuloendothelial cell activity.

How does it work?
By virtue of its particle size, intravenously injected colloidal technetium sulfide is primarily concentrated in the Kupffer cells of the liver (typically 80% or more), with the remainder localized in the spleen and bone marrow.

What are its advantages?
Because of a short 6-hour physical half-life and high useful radiation yield, high counting rates can be obtained with low radiation doses. Larger area scans can be carried out in reasonable periods of time without undue patient discomfort.

Why should I use this product?
(1) It's simpler than preparing your own. (2) Our technetium sulfide Tc 99m colloid is *gelatin*-stabilized —no anaphylactoid reactions have been reported. (3) NEISLER salesmen or specialists can service your needs in virtually all areas. And our Radio-pharmaceutical Customer Service Manager (phone 212-682-5057 or 212-682-5058) can provide technical service on any NEISLER radiopharmaceutical.
NOTE: AEC or state license required for the use of technetium sulfide Tc 99m colloid.

Indications—Liver, spleen, and bone scanning.

Warning—Should not be administered to pregnant or lactating women or to persons under 18 years unless, in the judgment of the physician, the situation requires its use.

As with all radiopharmaceuticals, dose should be limited to the smallest reasonable amount consistent with the greatest value in terms of relevant diagnostic information.

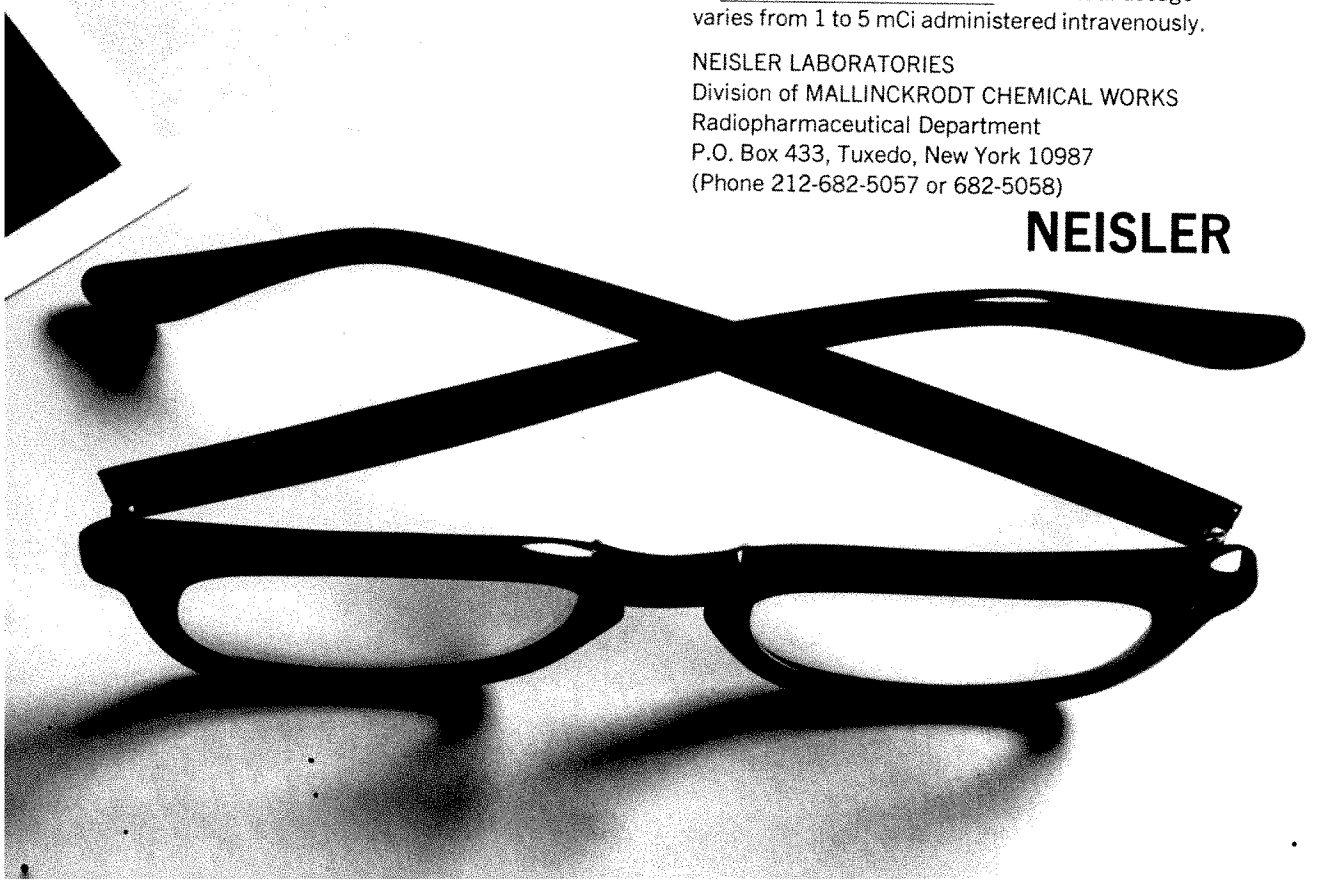
Precautions—Approved radiation safety precautions should be maintained at all times.

Adverse Reactions—None reported to date; however, patients should be carefully observed.

Dosage and Administration—The usual dosage varies from 1 to 5 mCi administered intravenously.

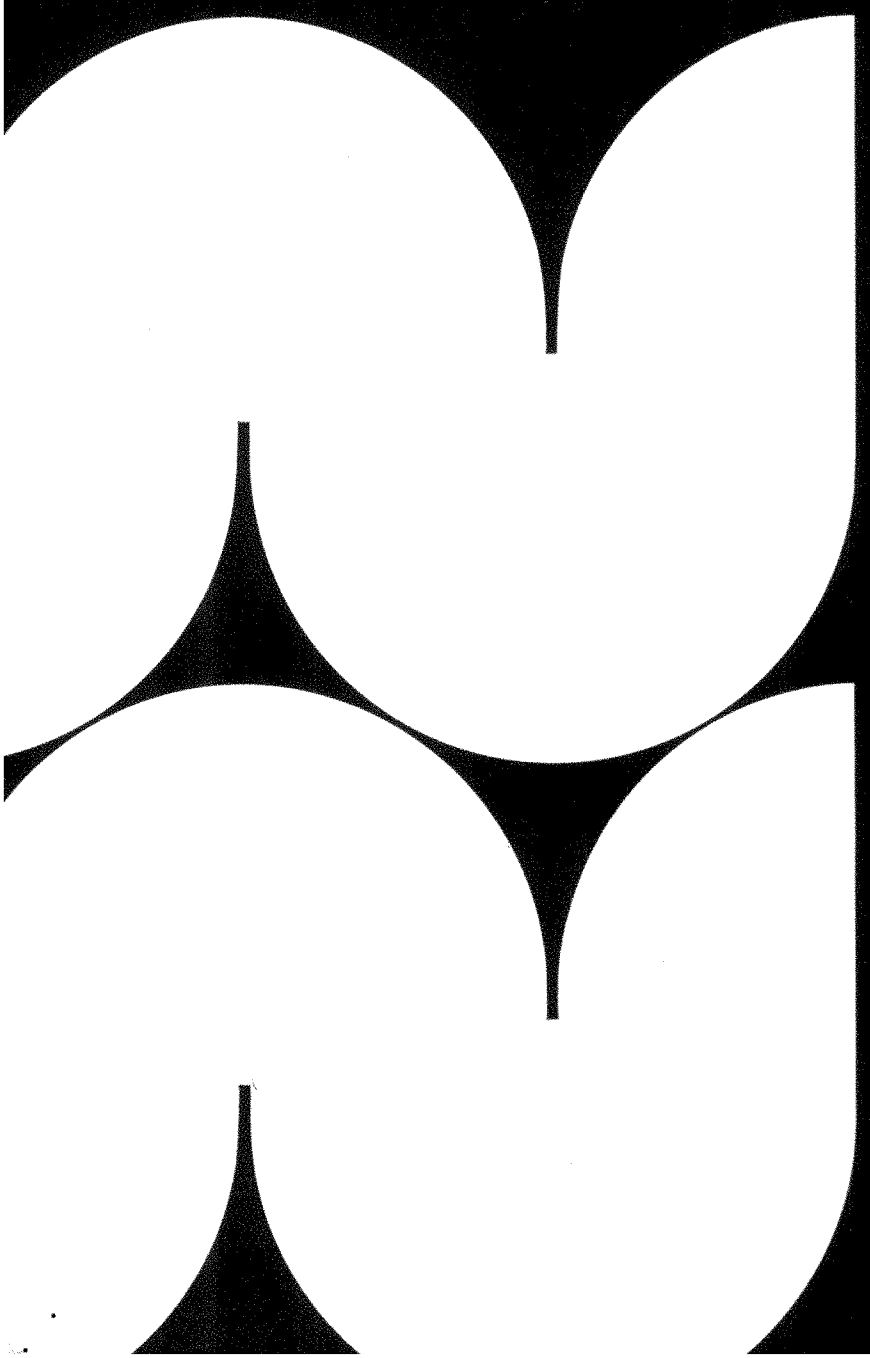
NEISLER LABORATORIES
Division of MALLINCKRODT CHEMICAL WORKS
Radiopharmaceutical Department
P.O. Box 433, Tuxedo, New York 10987
(Phone 212-682-5057 or 682-5058)

NEISLER



Micropaque®

arium sulfate
USP formulation



For optimum consistent definitic
by either route.

Oral
The smooth and palatable nature
of Micropaque is readily accepte
by all patients.

Enema
Micropaque completely coats
mucosal walls with an even
unbroken film to show up the
whole pattern.

Micropaque is available in
25 kilo drums and individual
examination packs for greater
convenience and economy.

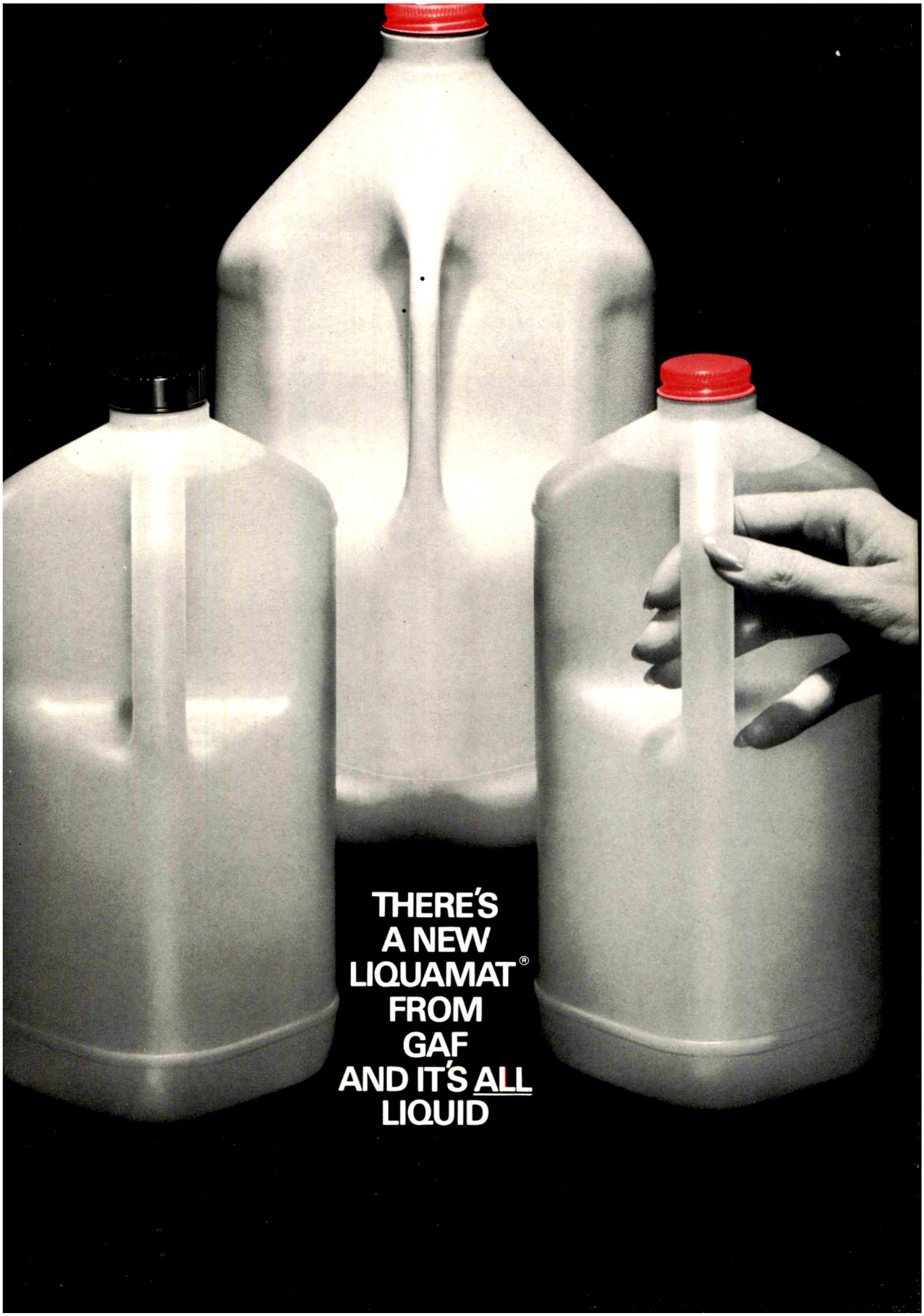
Micropaquettes®
contain 2 oz or 4 oz of Micropaq

Micropaque Disposable
Enema Kits
contain everything needed for
a single barium enema

Nicholas Laboratories Limited
180 East Post Road
White Plains New York 10601
Tel: 914 428-2544

Distributor in the U.S.A.
Picker X-ray

Manufactured by
Damancy and Company Limited
England


THERE'S
A NEW
LIQUAMAT®
FROM
GAF
AND IT'S ALL
LIQUID



Liquamat II, the all-liquid system designed for 90-second X-ray film processing.

It has everything you liked about the original Liquamat. Reliability. Cleanliness. Convenient packaging. All we did was move up the processing speed and take out the powder.

We didn't change anything else. Not even the price.

gaf®

GAF Corporation
140 West 51 Street, New York, N.Y. 10020

CONTROL....

All movements of HEAD, ARMS, COUCH and STRETCHER

now in the palm of your hand!



— for CONVENIENT, RAPID, RELIABLE PATIENT SETUP

NOW, the entire operation of an AECL THERATRON with the new, improved couch and stretcher is performed with a single hand control — an efficient, time saving device designed to ease the pressure on doctors and technicians. — Every movement is controlled with absolute precision by three dial knobs and one push button — all in the palm of your hand! Available now — telephone or write for details.

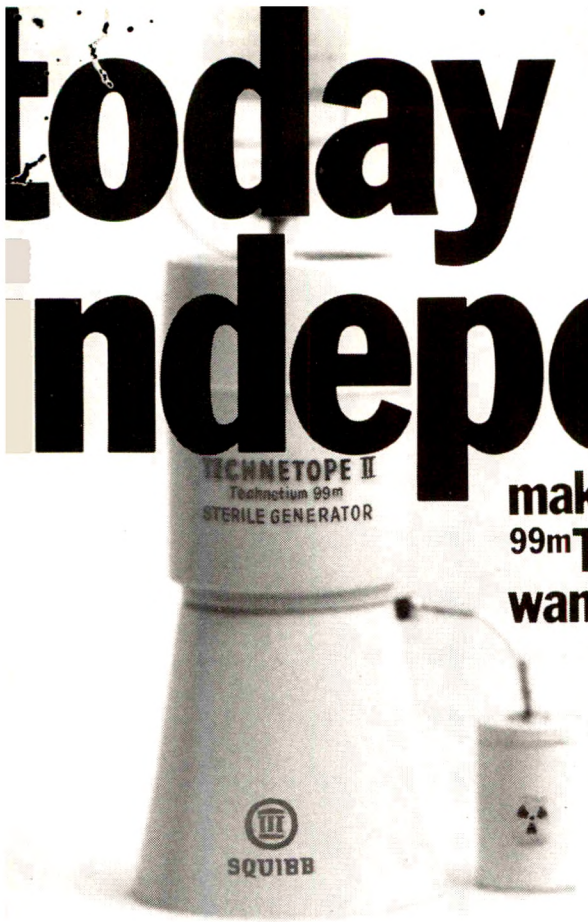
Atomic Energy of Canada Limited • Commercial Products

P.O. Box 93 Ottawa Canada

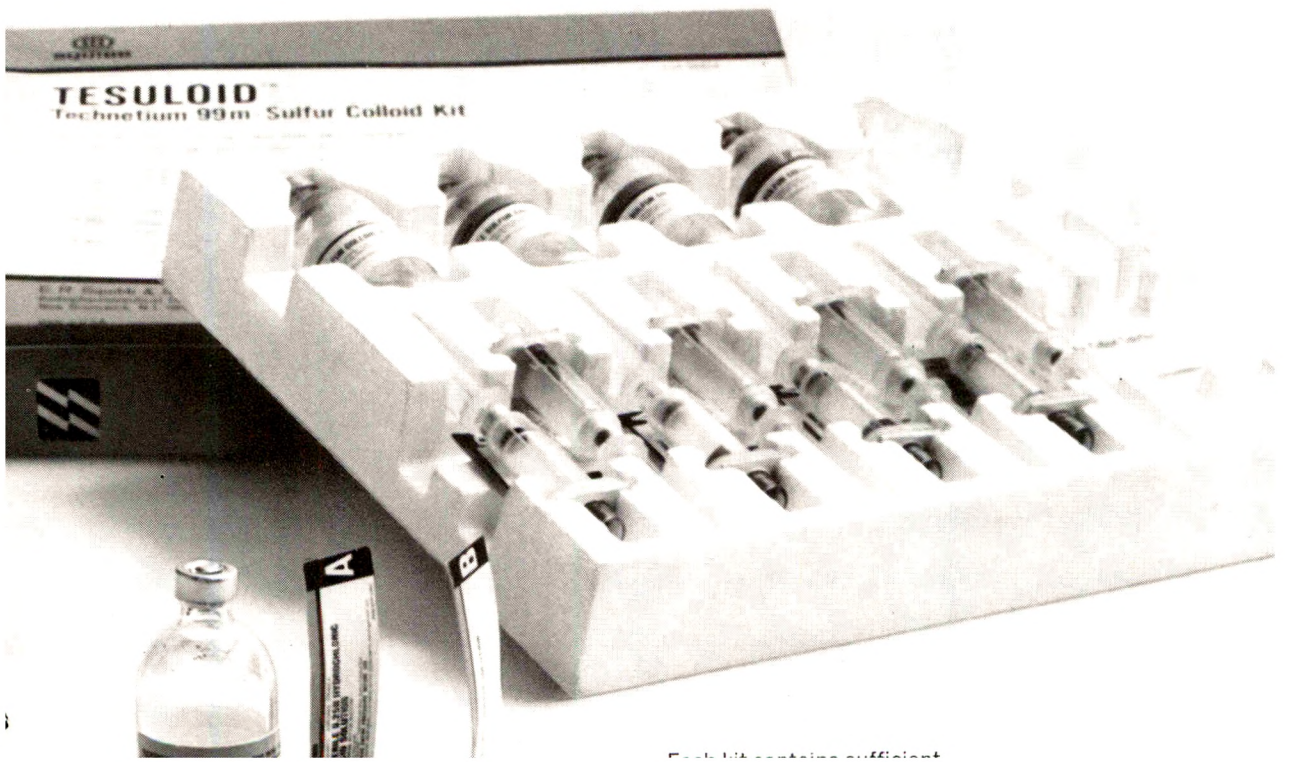
Telephone 613/836-2790 • Cable 'Nemeta'

69.1M

today be independent



make your own ^{99m}Tc Sulfur Colloid when you want it...when you need it



Each kit contains sufficient

New Tesuloid™

Technetium 99m–Sulfur Colloid Kit

...utilize ^{99m}Tc eluate from your sterile generator
...make as many doses as you want when you want
...keep dollar loss from product decay to a minimum
...more convenient and economical
...store kit anywhere – it's not radioactive*
...colloid contains no dextran...no rhenium

Package contains:

5 vials (3 cc. each) Sterile Sulfur Colloid Reaction Mixture. Each cc. of aqueous solution provides 4 mg. sodium thiosulfate, 3 mg. gelatin, 8.5 mg. potassium phosphate and 0.93 mg. disodium edetate. Contains no preservative.

5 UNIMATIC® Disposable Syringes (2 cc. each) of Sterile 0.25N Hydrochloric Acid Solution. Each cc. of aqueous solution provides 9 mg. hydrochloric acid.

5 UNIMATIC Disposable Syringes (2 cc. each) of Sterile Buffer Solution. Each cc. of aqueous solution provides 35 mg. sodium biphosphate and 10 mg. sodium hydroxide.

Warning: Solutions of sodium pertechnetate ^{99m}Tc withdrawn from the generator should always be adequately shielded. Early elutions from the generator are highly radioactive.

Precaution: Radiopharmaceuticals should not be administered to pregnant women or patients under 18 unless the information to be gained outweighs the hazards.

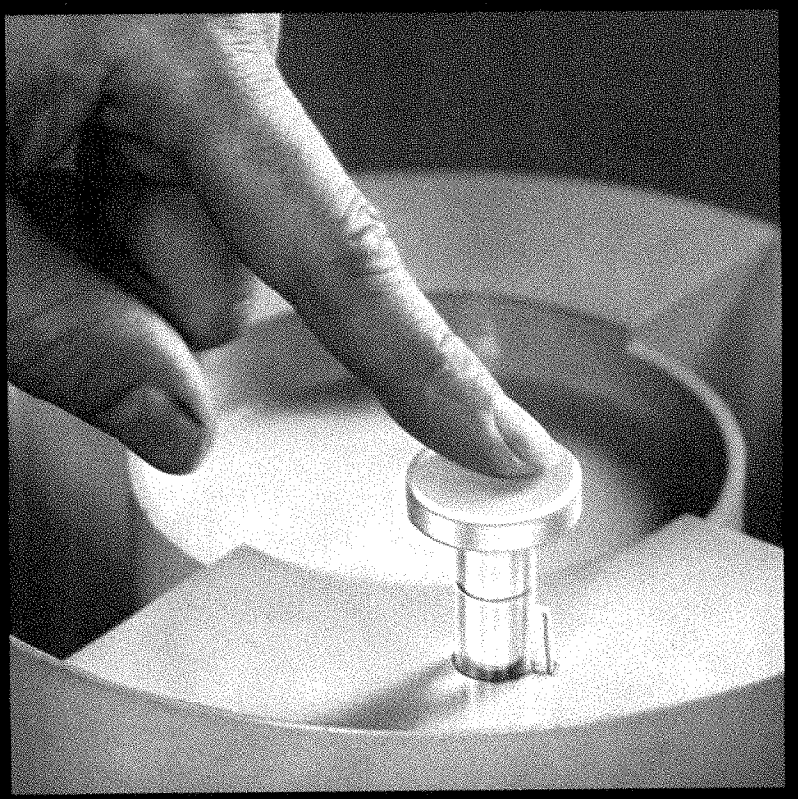
*However, adequate shielding of the Technetium 99m—Sulfur Colloid solution should be maintained.

Please send me complete information on new **Tesuloid**™ Technetium 99m—Sulfur Colloid Kit.

Please attach this coupon to your letterhead and mail to Medotopes Customer Service Department, P.O. Box #7, East Brunswick, New Jersey 08816.

Medotopes®

Push Button Milking



New faster way to daily production of ^{99m}Tc in your own laboratory

Jltra-TechneKow® Generato

Simplest way to produce sodium pertechnetate Tc99m
No assembly, no clamps, no generator manipulation.



ONLY 4 STEPS
IN THIS SIMPLE MILKING PROCEDURE

1. Attach sterile needle to plunger outlet.*
2. Place sterile, evacuated vial in elution safe and position it under needle.
3. Press plunger down so needle pierces diaphragm on evacuated vial; turn plunger slightly to lock in position. Milking will proceed automatically.
4. Release plunger to stop milking process. (Vial is now ready for calibration.)

*One needle serves for a full week. For sterility between milkings, retract needle and apply sterile needle cover.

Patent Applied For

The Mallinckrodt / Nuclear Ultra-TechneKow Generator is so modern, so simple to operate that any other system is antiquated, old fashioned, obsolete.

You receive the complete, plastic-enclosed Ultra-TechneKow Generator each week. No need to handle the generator or make tubing connections. When generator is exhausted, dispose of entire unit or return to Mallinckrodt for disposal.

Available in 4 activities:
50 mc 100 mc 200 mc 300 mc

Ask your Mallinckrodt/Nuclear Salesman for full information, or mail in the coupon.

MALLINCKRODT/NUCLEAR
Box 10172 • Lambert Field
St. Louis, Missouri 63145

Please send complete information on the new Mallinckrodt/Nuclear Ultra-TechneKow Generator.

Name (Please Print) _____

Position or Department _____

Laboratory or Hospital _____

Street _____

City _____ State _____ Zip _____

Mallinckrodt® NUCLEAR

RADIOPHARMACEUTICALS

MALLINCKRODT CHEMICAL WORKS
Box 10172 • Lambert Field
St. Louis, Missouri 63145
Atlanta • Chicago • Cleveland
Los Angeles • New York • Montreal

ROLLOSKOP

HIGH-CAPACITY FILM VIEWING DEVICE



The Rolloskop introduces a time and work saving method for the display of the X-ray films. It is based on a stationary illuminator unit and a mobile carriage for storage and transport of previously hung films. Identical units should be installed in pre-reading and demonstration rooms.

Immediately after processing, the radiographs for reading are hung on a transparent plastic band provided with clips. This band runs vertically over the illuminated area (57″ × 40″) on to spools in the top of the illuminator unit and in the carriage. The carriage with the films can be disengaged from the illuminator and transported to the viewing room where it is engaged to a second illuminator. Thus the films can be demonstrated in different places without being hung more than once. Radiographs can also be kept in spare carriages, e.g. for teaching purpose. Each spool takes up to 160 14″ × 17″ films.



ELEMA-SCHONANDER, INC.

Post Office Box 130 Mount Prospect, Illinois 60056

Roenten®



The preferred bowel evacuant — senna, purified and biologic assayed.

Clinical studies, based on 385 in-patients and 105 out-patier establish the efficiency and safety of Roenten as a bowel evacu prior to x-ray.

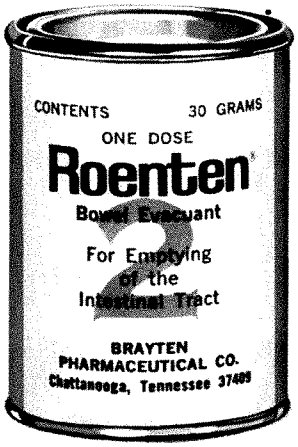
A Choice in Cleansing Strength to Meet Variable Patient Cont

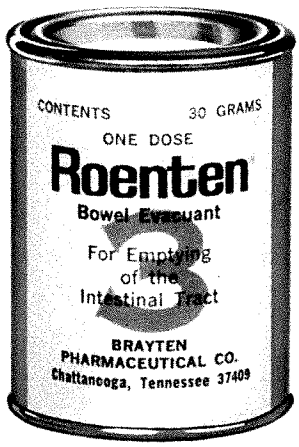
2-Gram Strength

Roenten® 2

Contains 2 grams of the active ingredient Senna (Cassia angustifolia) per 30 gram (1 oz.) dose. Found by Reavis, et al[1] to be comparable to castor oil in effectiveness as a bowel cleansing agent for radiography under **hospital control conditions.**

[1]Reavis, Charles W., et al, RADIOLOGY, Vol. 76, No. 4, Pages 642-643, April 1961



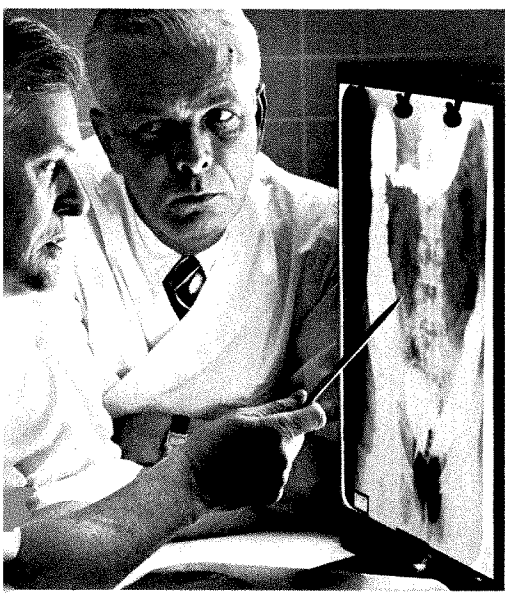


3-Gram Streng

Roenten®

Contains 3 grams of the activ gredient Senna (Cassia angusti per 30 gram (1 oz.) dose fo more difficult cleansing prot and variable control conditions.

DEPENDABLE



DEPENDABILITY: The preferred bowel evacuant, senna, purified and biologically assayed — in suspension assures rapid and complete bowel evacuation. Incidence of continuing spasm reduced.

Purified and Biologically Assayed, Cassia Angustifolia Senna Leaflets Blended with Agreeable Flavoring Agents.

Usual Dosage Directions

Contents of one container (30 Grams) stirred into three-quarters glass of milk or water, as physician directs, to make a readily acceptable drink which is the adult dose. Children take proportionately less as directed by the physician. When used to prepare for diagnostic X-ray it is taken at 4 or 7 P. M. (NO SUPPER) of the preceding day as directed.

CAUTION: Not to be used when abdominal pain, nausea, vomiting or other symptoms of appendicitis are present.

IMPORTANT: Frequent or prolonged use of this preparation may result in dependence on laxatives.

Samples for clinical evaluation supplied on request.

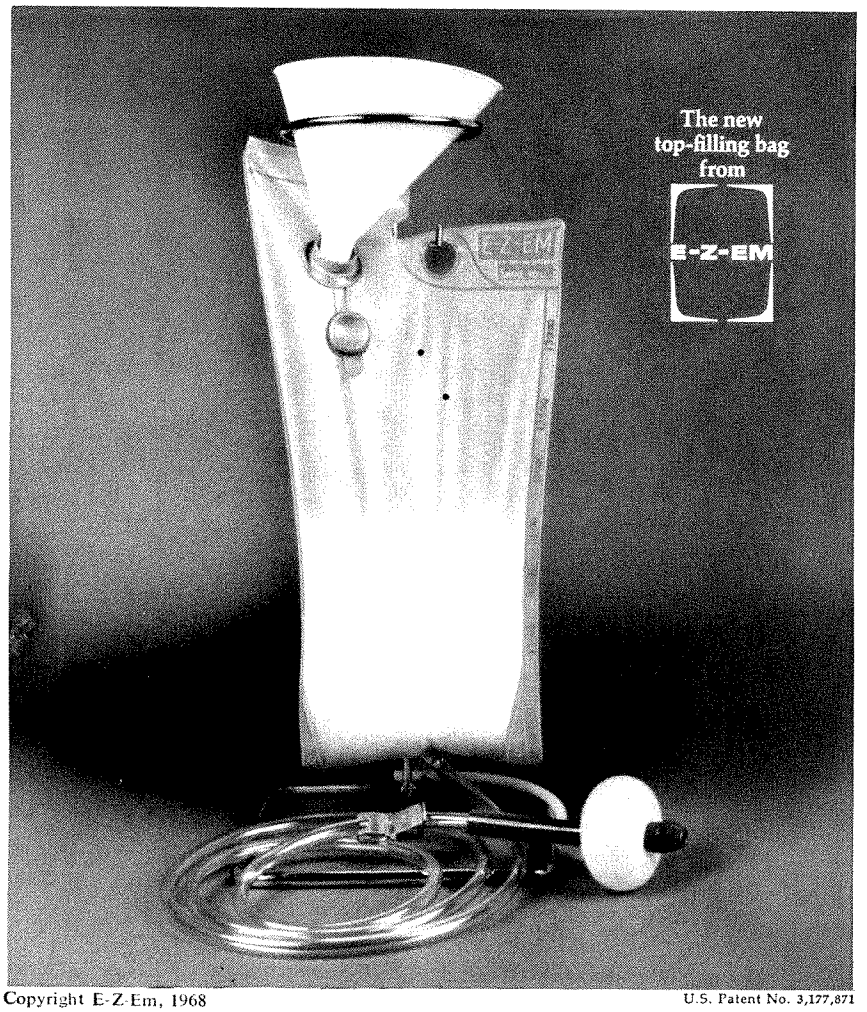
ACCEPTABLE



ACCEPTABILITY: The contents of one 30 gram co (1 oz.) stirred in ¾ glass of water or milk as you makes an attractive, really pleasant tasting, ch flavored non-oily suspension — invites the patient t the full dose.

Brayten PHARMACEUTICAL CO.
Division of Chattem Drug & Chemical Company
1715 W. 38th St., Chattanooga, Tenn. 37409

E-Z-EM'S NEW PATENTED RED TOP® SNAP-CLOSE BAG



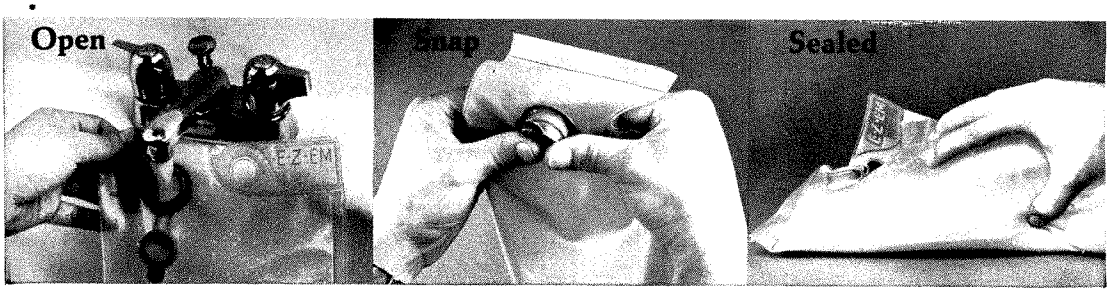
Copyright E-Z-Em, 1968 U.S. Patent No. 3,177,871

E-Z-Em's Open and Shut Case

(Prepackaged or Empty) E-Z-Em's Red Top™ disposable barium enema system combines the advantages of closed and open systems. The one piece patented Red Top™ seal opens up for fast filling and easy mixing — and allows you to add extra fluid during administration. Snapped shut, it forms a secure closed system, permitting fast drainage, introduction of gas for double contrast exams, and leakproof security withstanding over 600 pounds of pressure. The Red Ball™ at tube opening keeps the barium in the bag until administration. Only E-Z-Em is available either empty, or prepackaged with Sol-O-Pake™, or your own barium formula. Take your choice of tubing sizes and tips — conventional, Flexi-Tip™, or disposable retention tip. In stock at your local supplier.

E-Z-Em, 111 Swalm Street,
Westbury, N. Y. 11590. (516) 333-8230

Shown above: List 110 Red Top™, prepackaged, with rounded Flexicuff™



Improved reliability, even better performance.

Ohio Nuclear's new Model 84FD Dual Five, is the only scanner employing reliable, digital logic, computer-type electronics.

Speeds up to 750 cm./minute produce simultaneous, opposed view photoscans in less than half the time required by other scanners.

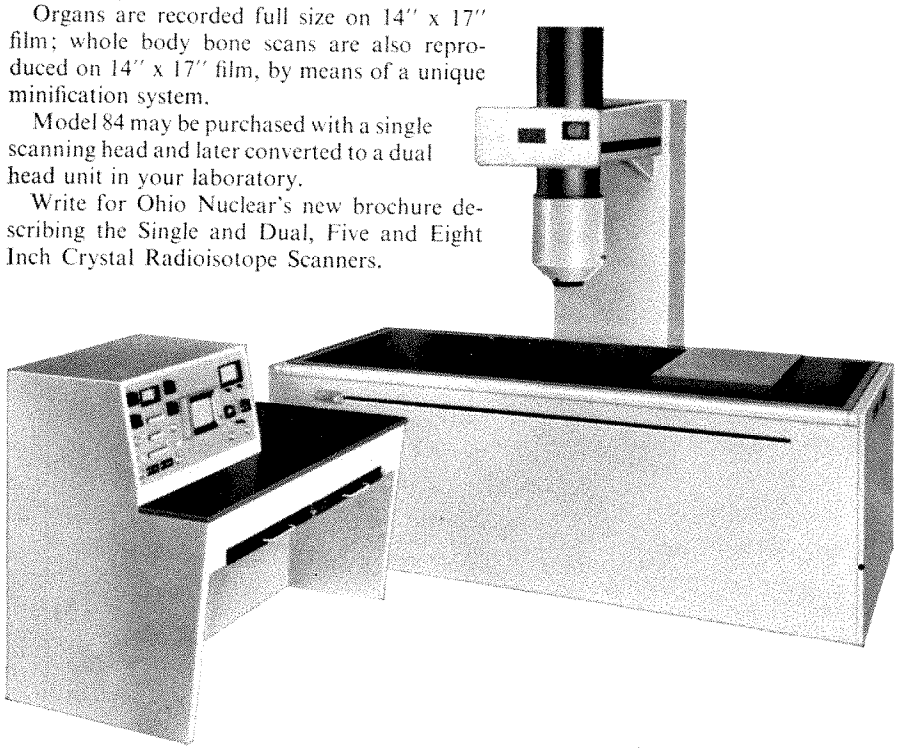
Scan progress is visually monitored on a storage cathode ray tube, which retains the organ image until manually erased.

Simplified pushbutton controls are conveniently located on the desk console. Photo Intensity Computer (PIC) circuit provides consistent, comparable maximum film density at the push of a button. Selectable levels of contrast enhancement and background erase accommodate individual preference.

Organs are recorded full size on 14" x 17" film; whole body bone scans are also reproduced on 14" x 17" film, by means of a unique minification system.

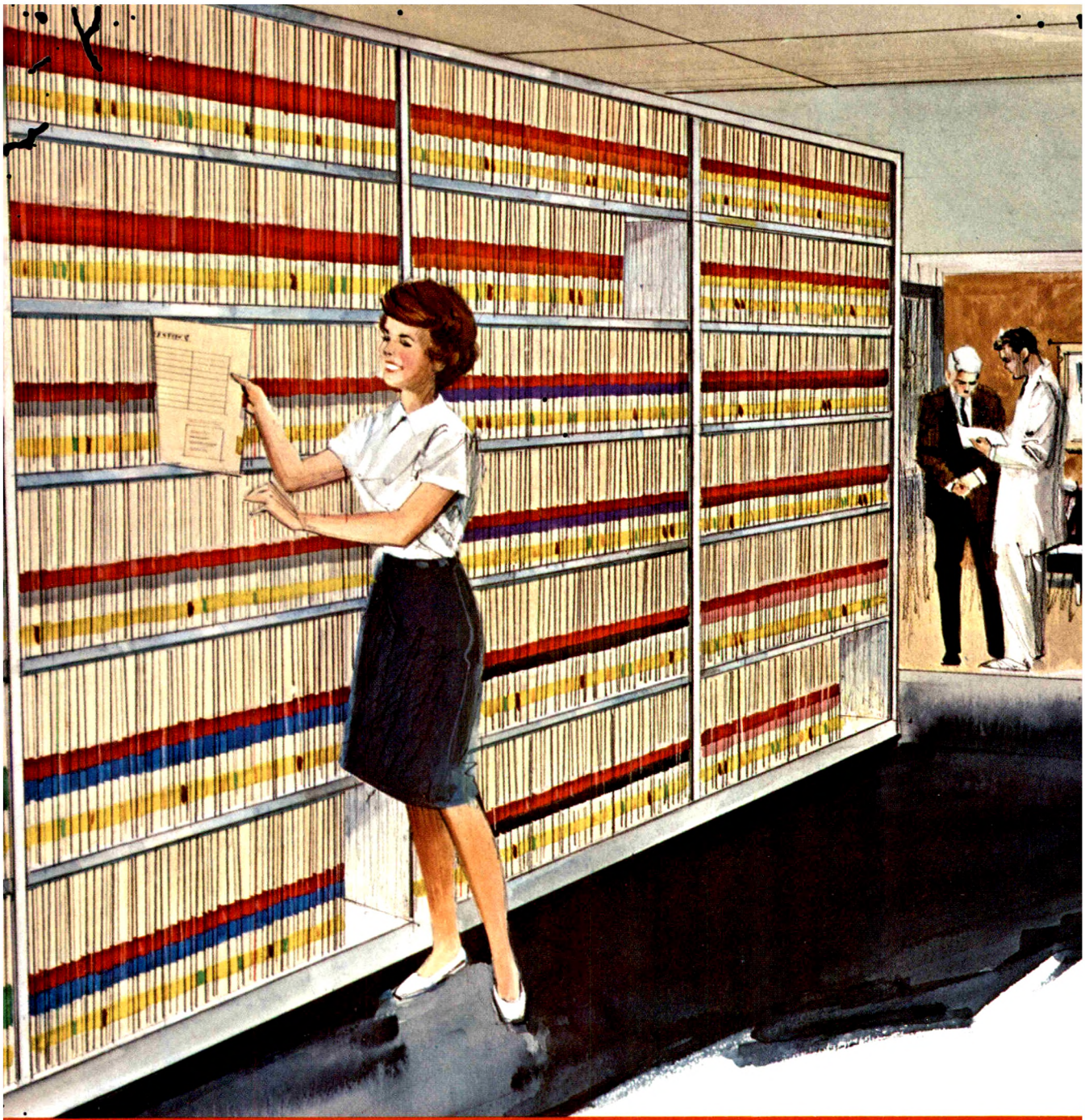
Model 84 may be purchased with a single scanning head and later converted to a dual head unit in your laboratory.

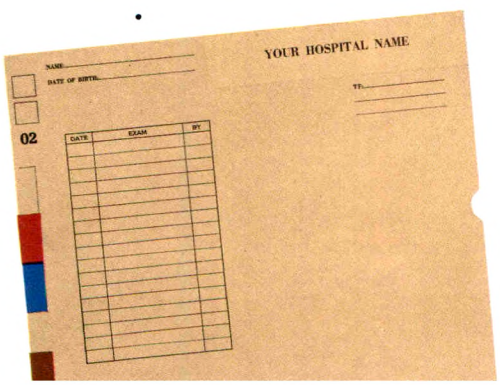
Write for Ohio Nuclear's new brochure describing the Single and Dual, Five and Eight Inch Crystal Radioisotope Scanners.

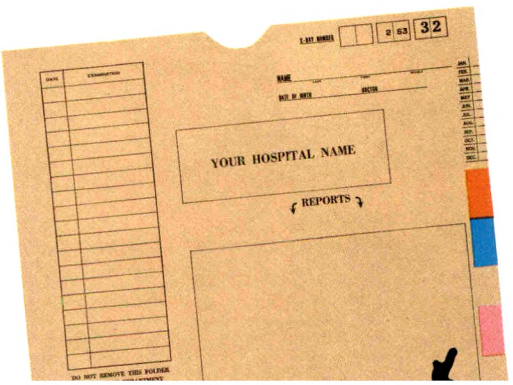


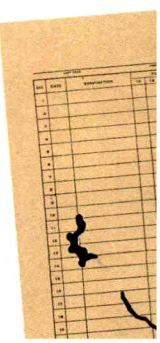
ohio-nuclear, inc.

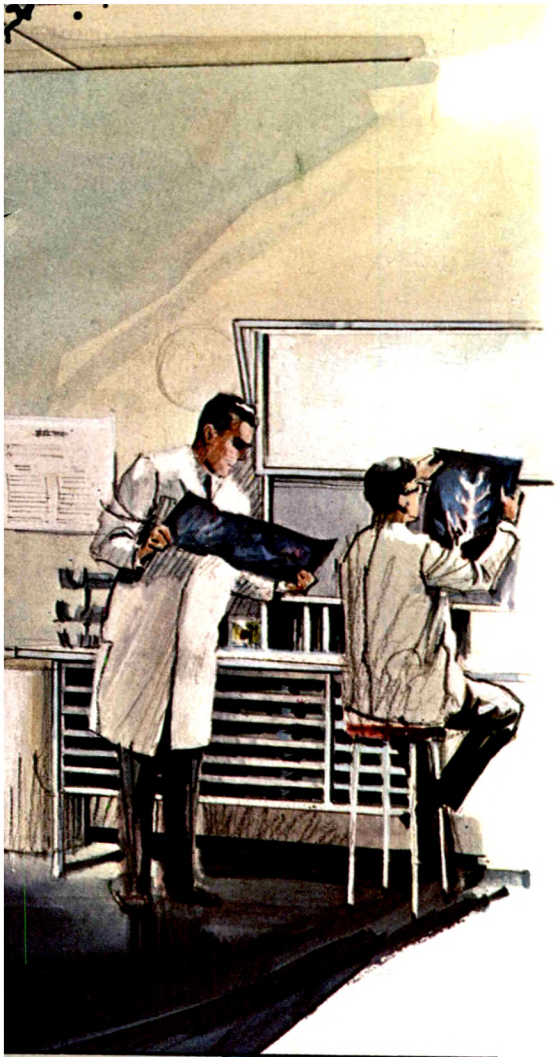
1725 Fall Avenue, Cleveland, Ohio 44113 (216) 621-8142




YOUR HOSPITAL NAME
NAME
DATE OF BIRTH
TEL
02
DATE
EXAM
BY


2 53 32
NAME
DATE OF BIRTH
DOCTOR
YOUR HOSPITAL NAME
REPORTS
DO NOT REMOVE THIS FOLDER





AMES COLOR-FILE eliminates mis-files in the Radiology Department

Color Coded X-Ray Jackets

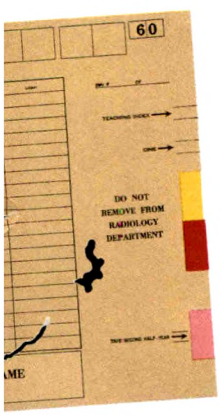
Two standard sizes are available:

14¾" x 18¼" open side
14¾" x 17¾" open end

Made from a durable tag, these jackets are printed in 10 colors in either two positions or three positions for terminal digit filing. The year code is also printed in color. Jackets are either pre-numbered with full unit number (when x-ray department issues its own number) or terminal digits only (when x-ray department uses hospital unit number). Terminal digits only may also be printed for use with Social Security numbers. Special pockets may be attached for reports.

Also available:

- Special sizes and styles
- "Teaching File" pockets available in various colors
- Expansion pockets for volumes; size 14¾" x 18¼" x 1"
- Open shelf guides
- Out guides



AMES COLOR-FILE CORPORATION
12 PARK STREET, SOMERVILLE, MASS. 02143 • TEL. (617) 776-1142

☐ Please have your representative call.
☐ Please send your new brochure on the advantages of color coding.
☐ Please send samples and prices on the following:

☐ X-Ray jackets ☐ Out guides ☐ Radiation therapy jackets
☐ Standard folders ☐ Special folders ☐ Consulting services

Quantity: (please check) ☐ 10M ☐ 20M ☐ 30M ☐ 40M ☐ 50M ☐ 100M ☐ Other

*Name*_____ *Title*_____

*Institution*_____

*Address*_____

*City*_____ *State*_____ *Zip*_____

*Area Code*_____ *Tel. No.*_____ *Ext.*_____

IMPORTANT!

OBTAIN MAXIMUM MARKET PRICES... from the nation's largest buyer of used x-ray film...

donald McElroy inc.

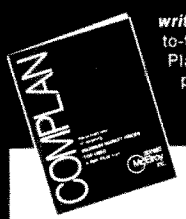
31 years of integrity

we purchase all brand and sizes of used x-ray film from anywhere in the United States . . . and we pay the freight cost.

we pay in advance if requested, or immediately upon the receipt and weight evaluation of your shipment.

our maximum market prices are gauged by the metals market and are adjusted continuously to reflect full value.

we offer 12-month, cumulative Incentive Payment Bonuses for consistent shipments of used x-ray film. You reduce storage problems, earn highest weight increment prices.



write for—your computerized, up-to-the-hour Quotation for Purchase Plan that assures you of our pledge to give . . . Maximum Market Prices.

DONALD McELROY INC.
3201 old glenview road
wilmette, illinois 60091

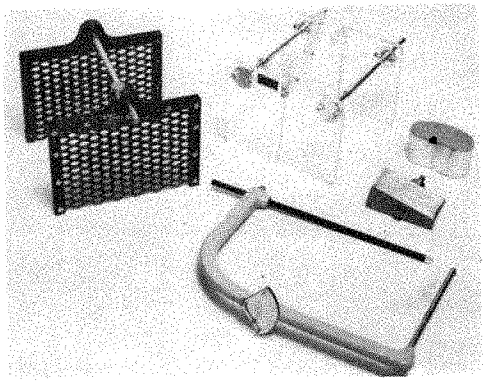
Please send me COMPLAN TODAY.

NAME

ADDRESS

CITY STATE ZIP

new from BARUCH



$7 and up.

$7 buys our smallest lead block—$95 buys a Cervical/Rectal Localizing Caliper —$105, a Compression Breast Bridge— and $3350, our motor-driven therapy positioning chair with head support assembly. And in between, we have the broadest existing line of radiation therapy accessories and devices to save personnel time and contribute to the highest standards of patient care.

For that $7 you really get your money's worth. The block is encased in polished brass to prevent distortions, with a Naugahyde covering top and bottom to protect the table top from scratches. It's one of an assortment of 64 standard sizes of beam trimming blocks. We also make a BeamBlock Table on which you can arrange them, support them, and store them. It's quite a help.

All of our products are that way.

Ask us for literature describing these and other accessories for radiation therapy—Baruch specializes in solving your therapy equipment problems.

BARUCH INSTRUMENTS CORPORATION
203 North Highland Avenue
Ossining, N.Y. 10562
(914) 762-2255

SQUIBB

a research concept in contrast visualization

for better definition of disease: documenting differences between contrast agents

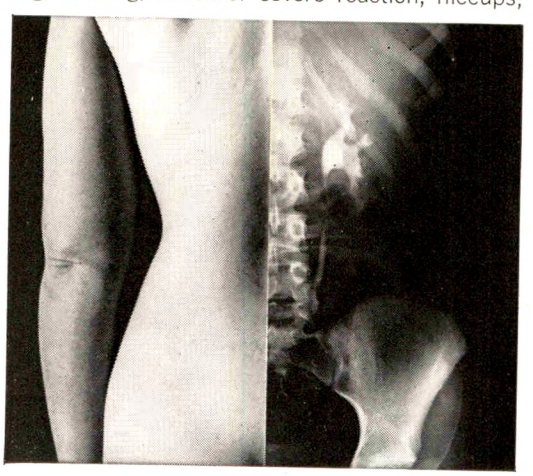
No. 1 in a series:

Renografin-60 (meglumine diatrizoate injection) preferred in a study of pyelographies of 2,234 patients.

In a new large scale study,[1] "...to determine which medium would produce adequate visualization of the urinary tract with the fewest toxic effects on the patient," Macht *et al.* have compared Renografin-60 with 2 other contrast agents.

Data were analyzed in 2,234 unselected (consecutive) patients, according to age, sex, and general disease group for the study population as a whole. The first 683 patients received 50% diatrizoate sodium solution, the next 921 patients received Renografin-60, and the final 630 patients received 66.8% sodium iothalamate solution.[1]

criteria for quality and comparative safety The contrast agents were evaluated for quality of diagnostic films as follows: films showing a dense concentration of contrast medium with filling and visualization of all major and minor calyces, infundibula, pelves and almost all of each ureter were listed as "good"; films showing less concentration with incomplete visualization of all portions of urinary tract but sufficient to produce diagnostically adequate films were listed as "fair"; films showing unsatisfactory visualization of urinary tract, or films which could not be interpreted, as "poor." The media were also evaluated as to incidence of the following side effects: nausea, vomiting, fainting, shock or severe reaction, hiccups, hives, pain in arm, sneezing, hot flushes, stuffiness of nose or ears.[1]



The following chart* shows comparative results of the 3 media according to age category:

quality of pyelograms and side effects expected in standard population of 1,000 patients by age, according to type of medium used

medium used and type of patient	standard population	quality of pyelograms good	fair	poor	with side effects
meglumine diatrizoate					
all ages,	1,000	827	123	50	41
0-19†	126	122	3	1	3
20-49	415	374	35	6	27
50-69	315	240	51	24	9
70 or older	144	91	34	19	2
diatrizoate sodium					
all ages,	1,000	782	134	84	72
0-19	126	115	6	5	7
20-49	415	378	26	11	40
50-69	315	227	64	24	19
70 or older	144	62	38	44	6
sodium iothalamate					
all ages,	1,000	883	81	36	54
0-19	126	122	4	0	7
20-49	415	393	20	2	29
50-69	315	269	32	14	13
70 or older	144	99	25	20	5

*Adapted from Macht[1] †In some patients in this age group, higher than recommended doses were used.

In theory: "The choice of contrast agent should ideally be individualized according to the age, sex, and disease group of the patient in order to obtain a high probability of complete visualization of the urinary tract with low probability of adverse side effects."[1]

In practice: "The choice is to be made...on the basis of the agent which gives the best concentration and the fewest side effects in the greatest number of patients regardless of age, sex, or disease category."[1]

In order of preference: Although Renografin-60 was not rated highest in all categories, the authors feel that their preference of the contrast media for intravenous pyelography would be: first, Renografin-60; second, sodium iothalamate; third, diatrizoate sodium.[1]

For brief summary of prescribing information, please refer to the end of this advertisement.

definition of safety...

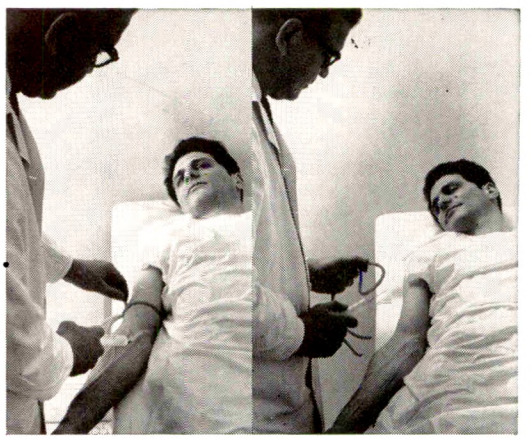
demonstrated in animals... Since meglumine diatrizoate is also used for cerebral angiography, toxicity studies of administration via the carotid artery are therefore of interest. Fischer and Eckstein[2] designed angiographic studies in animals in which procedures were very similar to clinical angiography, and which yielded data that was quantitative, graphic and nonsubjective.[2] According to the authors: "We selected the alterations in arterial blood pressure, venous pressure, heart rate and rhythm, the electrocardiogram and end-expiratory CO_2 concentration resulting from experimental cerebral angiography as refined, sensitive indications of the toxicity of a particular contrast material."[2] Their results of measured cardiovascular functions in dogs indicated that meglumine diatrizoate was far less toxic than four other contrast media.[2] As Fischer and Cornell reported in a later study: "Despite the testing of more highly concentrated solutions and larger doses, the cardiovascular responses [in dogs] from methylglucamine [meglumine] salts were much less than from sodium salts, an observation consistent with previous experiments."[3]

Other investigators have documented the comparative safety of meglumine salts in experimental studies. In order to determine reaction and tolerance of the intestines, Cooley[4] injected meglumine diatrizoate into mesenteric arteries of dogs and found no damage. Gensini *et al.*[5] reported that cardiovascular responses with it were almost identical to blood transfusions.

theory of lower toxicity with meglumine... Gensini and DiGiorgi have offered a hypothesis to explain their findings of lesser toxicity with experimental intravascular injections of methylglucamine (meglumine) salts. "When a relatively undiluted amount of sodium salts of a contrast agent is injected in an artery and carried by the blood stream toward the capillary bed, its molecules rapidly dissociate and readily diffuse through the capillary membrane and into the tissue. There, both the toxic effect of the iodine-containing organic radical and the increased concentration of sodium will readily manifest themselves. At equal concentrations of sodium, the end results will closely reflect the intrinsic toxicity of the iodine-containing organic radical on the tissues...."[5]

"In the case of the methylglucamine compounds, the same dissociation takes place. However the larger methylglucamine molecule, rich in hydrogen bonds, apparently either limits the migration of the organic radicals outside the vessel or at least minimizes their effects on the cellular metabolism."[5]

proved in practice... Paralleling similar findings in animals, clinicians have reported a generally lower



incidence of untoward reactions with Renografin-60 in urologic and cerebrovascular use. However, as with all intravascularly injected contrast agents, the possibility of severe reactions should be kept in mind (see Contraindications, Precautions and Side Effects below). In one study of over 600 urologic patients, the investigators reported that Renografin-60 produced urograms of diagnostic quality with a 6% incidence of side effects. The authors concluded: "It is hard to believe that any drug introduced intravenously could be so well borne by so many patients...."[6]

In a 74-patient study,[7] comparing Renografin-60 with diatrizoate sodium in carotid arteriography, Shealy commented: "With confused patients who are to have arteriography under local anesthesia, it is particularly desirable to have an agent that causes little pain." In this study, since "...60 per cent Renografin has resulted in considerably less pain than 50 per cent or 45 per cent [diatrizoate sodium]...we have converted to the routine use of 60 per cent Renografin for carotid arteriography; an additional 1,500 arteriograms done with 60 per cent Renografin have been quite satisfactory."[7]

better tolerated even in pediatrics... Citing some difficulties in administering contrast agents intravenously to children, Strasser *et al.*[8] selected Renografin-60 for intramuscular use in excretion urography in 16 pediatric patients because of the mild and relatively few reactions consistently associated with its use. The authors concluded: "The almost complete absence of any kind of local effect from its injection into the gluteal muscle and the absence of any serious reactions, local or systemic, indicate the safety of the medium."[8]

For brief summary of prescribing information please refer to the end of this advertisement.

definition of efficacy...

a thoroughly investigated meglumine salt Extensively evaluated for over a decade, Renografin has been consistently shown to yield a high percentage of diagnostic quality films in many phases of contrast visualization.

Upon intravenous injection, Renografin is rapidly carried to the kidneys and is so well concentrated that renal passages—including renal pelvis, ureters and bladder—may be clearly visualized. This medium also provides high contrast vasography in visualization of the cerebral vessels and the peripheral arteries and veins.

proved diagnostic excellence... In a comparative study[9] of 3 contrast agents used in cerebral angiography by Doehner (comprising a cross section of an average neurosurgical practice), Renografin-60 was equal in the arterial phase and slightly superior in the venous phase of the examination.

Findings of a previously cited study by Orr *et al.*,[6] in intravenous pyelography, also attest to the diagnostic excellence of Renografin-60. "Satisfactory roentgenograms of the kidneys were obtained in 636 (97%) of the cases, demonstrating the great diagnostic value of this procedure." And, as noted previously, Shealy found the contrast agent to be "quite satisfactory" in 1,500 carotid arteriograms.[7]

References: 1. Macht, S. H.; Williams, R. H., and Lawrence, P. S.: Amer. J. Roentgen. *98*:79 (Sept.) 1966. **2.** Fischer, H. W., and Eckstein, J. W.: Amer. J. Roentgen. *86*:166 (July) 1961. **3.** Fischer, H. W., and Cornell, S. H.: Radiology *85*:1013 (Dec.) 1965. **4.** Cooley, R. N., *et al.*: Angiology *15*:107 (Mar.) 1964. **5.** Gensini, G. G., and DiGiorgi, S.: Radiology *82*:24 (Jan.) 1964. **6.** Orr, L. M.; Campbell, J. L., and Thomley, M. W.: J.A.M.A. *169*:1156 (Mar.) 1959. **7.** Shealy, C. N.: J. Neurosurg. *20*:137 (Feb.) 1963. **8.** Strasser, N. F., *et al.*: Radiology *79*:408 (Sept.) 1962. **9.** Doehner, G. A., and Brugger, G. E.: New York J. Med. *60*:4022 (Dec.) 1960.

Contraindication

A history of sensitivity to iodine per se or to other contrast media is not an absolute contraindication to the use of meglumine diatrizoate.

Precautions and Side Effects

Severe, life-threatening reactions are rare; when they occur they suggest hypersensitivity. A personal or family history of asthma or allergy warrants special attention and may predict, more accurately than pretesting, the likelihood of a reaction, although not the type nor severity of the reaction in the individual.

The value of any pretest is questionable. The pretest most performed is the slow injection of 0.5-1.0 cc. of the preparation into a peripheral vein. An impending reaction is often indicated by transient burning and flushing, pain, "jump-like" reactions, respiratory difficulty, faintness, sneezing, itching, nausea, vomiting or urticaria. Should the test dose produce an untoward response, the necessity for continuing the examination should be re-evaluated. Antiallergic drugs may be used to advantage. In a few cases, the reactions to the test dose have been extremely severe.

The more serious anaphylactoid reaction requires immediate treatment and may occur despite a negative sensitivity test. An emergency tray consisting of vasopressor drugs, epinephrine hydrochloride 1:1000, methoxamine (Vasoxyl) or metaraminol bitartrate (Aramine), and glucose and saline is recommended. Oxygen and instruments to guarantee a clear airway must be readily available.

Caution must be exercised, especially in cerebral angiography in extreme age, in severely debilitated patients and in those with marked or severe hypertension, advanced arteriosclerosis, cardiac decompensation, recent cerebral embolism, or thrombosis, chronic pulmonary emphysema and in cyanotic infants.

For full details the Package Insert should be read.

Supply: Renografin-60 is supplied in vials and ampuls as a sterile aqueous solution providing 60% meglumine diatrizoate containing approximately 29% firmly bound iodine.

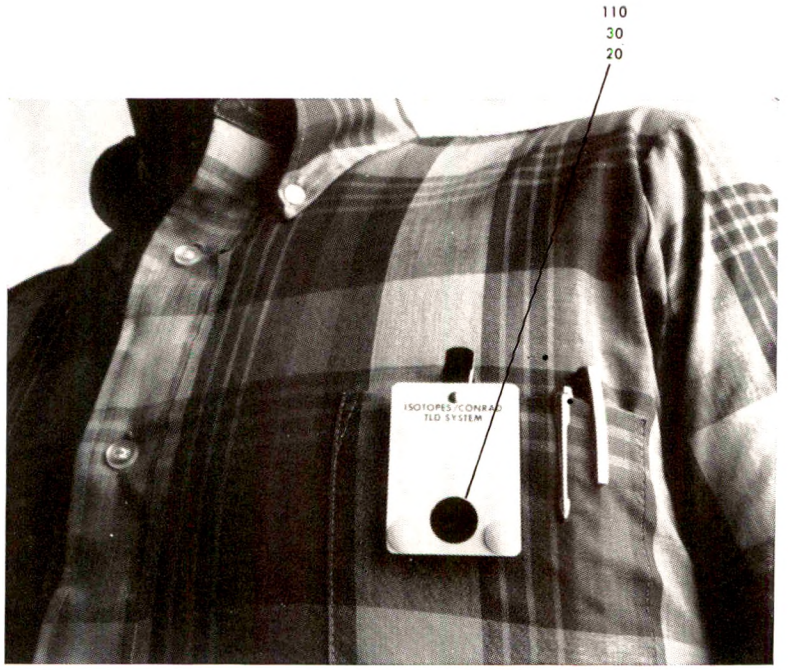
Available in 30 cc. vials or 25 cc. ampuls.

in excretion urography
cerebral angiography
peripheral arteriography
and venography

Renografin®-60

Squibb Meglumine Diatrizoate Injection U.S.P.

SQUIBB 'The Priceless Ingredient' of every product is the honor and integrity of its maker.



ISOTOPES NEW TLD BADGE SERVICE CAN TELL YOU A LOT MORE ABOUT YOURSELF.

Accurately, directly and fast. And in biologically significant terms. That's because the three tissue-equivalent LiF discs in an ISOTOPES TLD Badge are calibrated to tell you the precise dose to the skin, gonads and bone marrow. Then our TLD Readout Instrument prints out these dose records within a few minutes. No film processing, no checking calibration curves, no attempts at interpreting organ doses and no waiting as with film badges.

But there's even more. TLD Badges have a very broad dose range, 10 mrad to 10^5 rads. Particularly significant in accidents where immediate readout is vital. At the same time, the stability of TLD Badges over long periods of time recommends their use for low risk personnel, too.

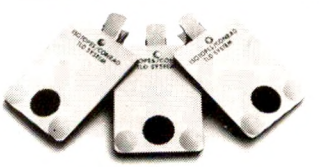
The Badge is extremely rugged, unaffected by temperature extremes, humidity, mechanical shock, light, water and most common solvents.

All in all, its ease of measurement and interpretation, long measuring periods and fast readout make savings possible for many categories of personnel whose doses are now monitored with film badges.

ISOTOPES TLD Badge Service is at your service. However, if you want to set up your own TLD Badge System with your own readout capability, we can help you do that, too. In either case, call or write ISOTOPES, 50 Van Buren Avenue, Westwood, N.J. 07675, (201) 664-7070.

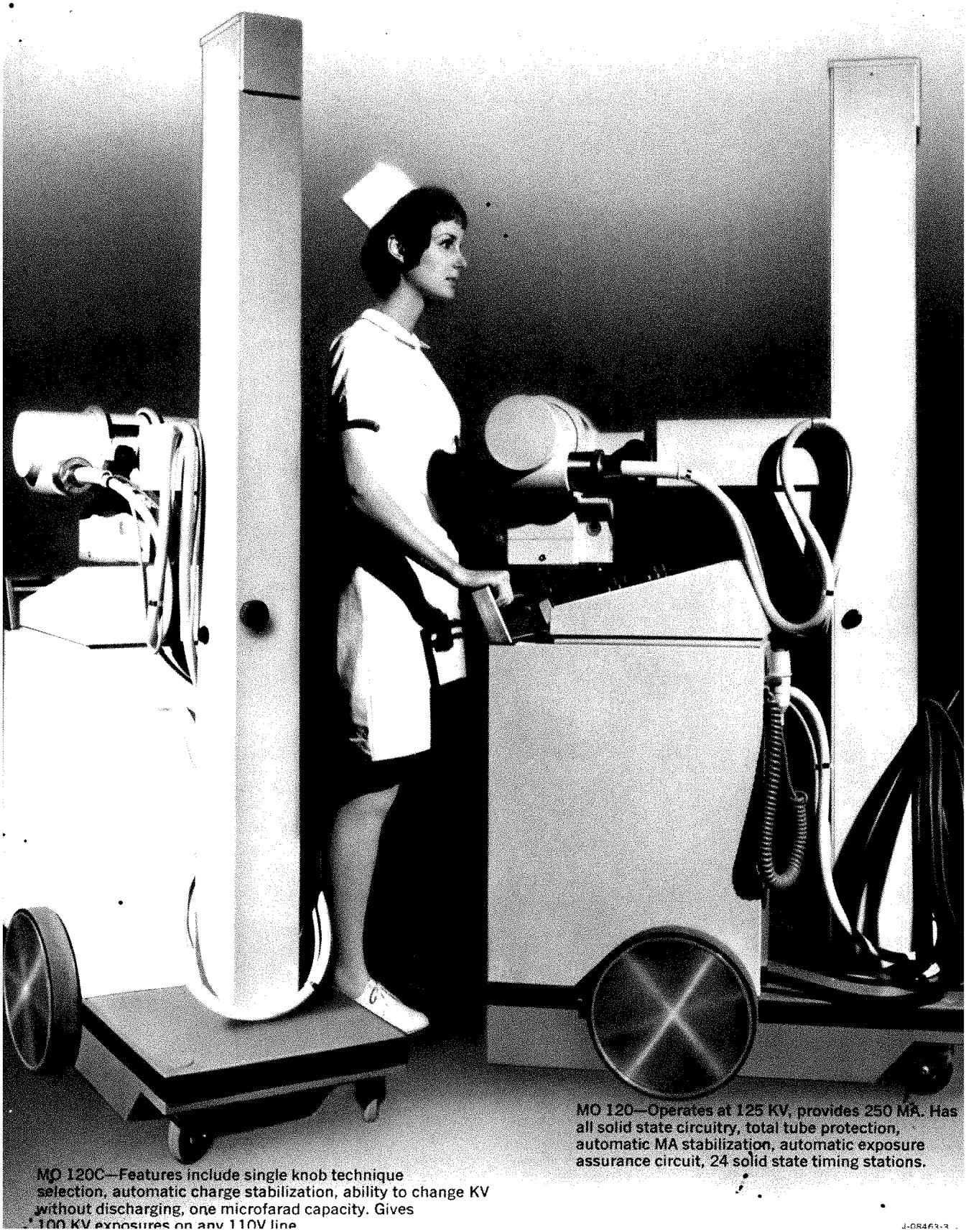
ISOTOPES

A TELEDYNE COMPANY




Meet the
X-ray twins
anyone can
push around.

The Lightest Weight X-Ray Mobiles. From Westinghouse.



MO 120—Operates at 125 KV, provides 250 MA. Has all solid state circuitry, total tube protection, automatic MA stabilization, automatic exposure assurance circuit, 24 solid state timing stations.

MO 120C—Features include single knob technique selection, automatic charge stabilization, ability to change KV without discharging, one microfarad capacity. Gives 100 KV exposures on any 110V line.

J-08463-3

When we say mobiles, we mean the smallest technician can wheel them around as easily as a supermarket cart. Our MO 120 for 220 V operation weighs in at 500 lbs.; our MO 120C condenser discharge unit for 110V operation tips the beam at 550 lbs.

Both are far lighter than any other leading mobiles. But in radiology use they're worth their weight in gold. Low profile, so you don't need a guide to move them around.

For a demonstration or full details on the Westinghouse mobiles that can go anywhere as easily as you can, write or call our nearest sales office or Westinghouse X-Ray Division, 2519 Wilkens Avenue, Baltimore, Maryland 21203.



You can be sure... if it's

Westinghouse

When we can't take a giant step, we take little ones.

B-D has been supplying the medical profession with surgical, diagnostic and therapeutic products of the highest quality since 1897.

The B-D name is a synonym for half a hundred practical advances in hospital and laboratory techniques. Like needles with specially-angled side bevels for consistent sharpness. Syringes with a positive lock that prevents accidental needle separation.

And disposability.

B-D also has long worked hand-in-hand with physicians and surgeons to develop variations in needles and instruments to meet their specific requirements.

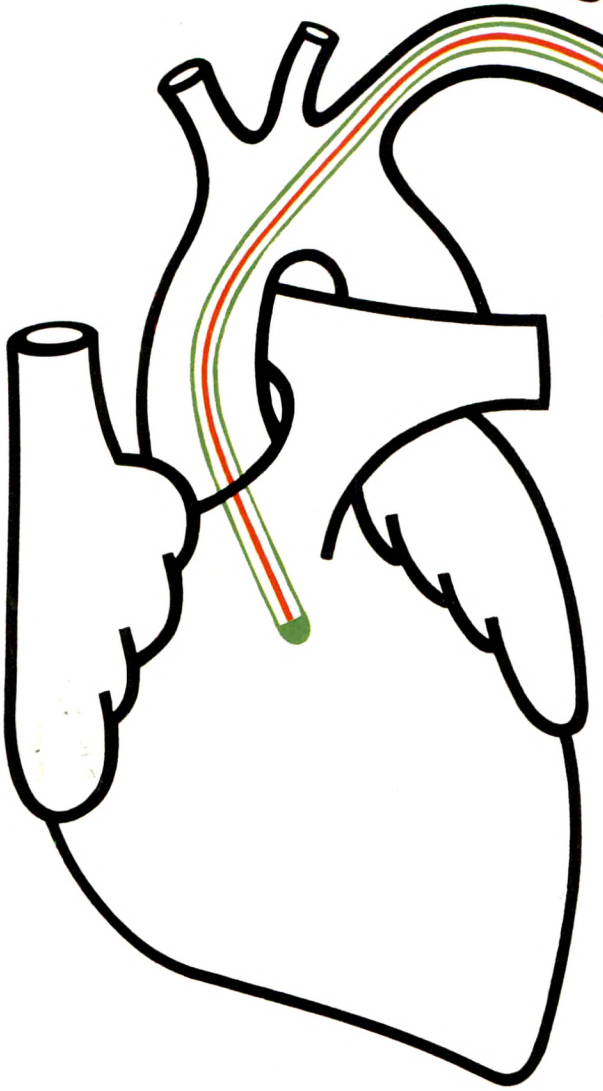
When we can't take a giant step, we take little ones. Carefully controlled steps, with infinite attention to detail. Always in the same direction. Always aimed at freeing skilled hands from needless routine ... at making it easier for you to use your skill to the fullest.

That's why everything changes at B-D but our name.

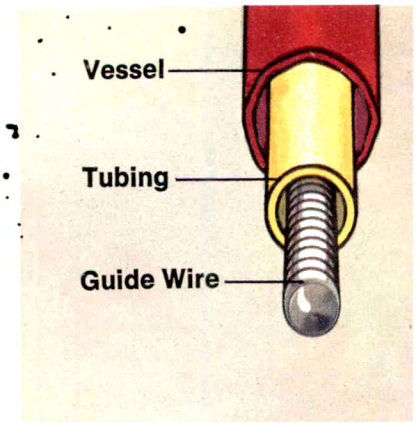
B-D

A step ahead in patient care.

B-D GETS TO THE HEART OF THE MATTER.



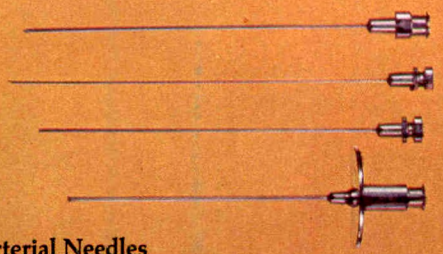
B-D engineering skills continue to improve instrumentation for all vascular and catheterization procedures. As new techniques are conceived for exploring inner space, look to B-D for the products to make them practical, safer and simpler to perform.



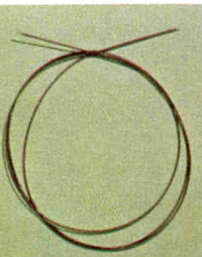
Precision products for arterial and venous catheterization.

B-D offers you a wide range of arterial and venous catheterization components for use in the Seldinger Technique of percutaneous catheterization . . . plus accessory items used in angiographic procedures. These products are precision made under the most exacting requirements to make sure that you have the safest instruments possible, capable of producing the most satisfactory results.

The Seldinger Technique eliminates the need for cutdown and arterial suturing, minimizes blood leakage as the catheter dilates the blood vessel. There's less trauma to the blood vessel; less discomfort for the patient. And the contrast medium may be injected at any desired level. In this procedure, the catheter is advanced over a flexible, stainless steel spring guide wire which had been previously introduced through a needle. Fixed or movable tapered inner cores facilitate easy passage within the blood vessel. (See illustration at left.)



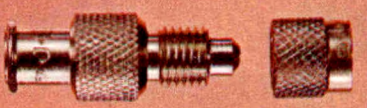
Arterial Needles
Designed for accuracy and ease of handling. Consists of thin-wall outer cannula with blunt tapered point and LUER-LOK hub, an inner cannula with short bevel point and fitted stylet. Plus a blunt, rounded obturator for the outer cannula.



SAFEGUIDE Guide Wires
Provide added flexibility, safety, convenience. Made of special stainless steel alloy. Tapered inner core available on both fixed and movable core designs... eliminates problems of stretching or kinking. Protective polypropylene holder coil.



FORMOCATH Radiopaque Polyethylene Tubing
Especially fabricated for use with SAFEGUIDE Guide Wires. Excellent flexibility with maximum torque... minimizes trauma, maximizes maneuverability. Readily flared and formed to individual requirements. Wide variety of thin-wall and heavy-wall sizes.



LUER-LOK Flare-type Adapters and Stopcocks
Reusable metal adapters and stopcocks for polyethylene tubing with a flare-type connection and screw cap for fastening tubing securely. Available with both male and female LUER-LOK attachment. Will accommodate tubing up to 11 French.

The arterial and venous catheterization components pictured above are available in a variety of sizes. Also available are accessory products used in angiography procedures. These include Cope 3-way adapter-forming wires (for sizing and shaping catheter tips), flaring tool and hole punch set (for fabricating catheters), and various disposable and reusable roentgenography sets to meet your pressure requirements. Available from your local surgical supply distributor.

BECTON-DICKINSON
Rutherford, New Jersey 07070
Division of Becton, Dickinson and Company

B-D, FORMOCATH, LUER-LOK AND SAFEGUIDE ARE TRADEMARKS. PRINTED IN U.S.A. 40768

B-D

A step ahead in patient care.

It's what's in between that counts...

If you're doing special procedures and need a particularly fine x-ray grid providing freedom from mottling and with almost invisible lines in the film image, choose the L-F Ultralūm and Micralūm Grids. For all stationary grid uses where clarity requirements are critical, these Grids are ideal. They are practically pattern-free and are used, in some cases, in lieu of a moving Bucky Grid. Yes—it's what's in between that makes the difference... it's the aluminum interspacers that give you this less noticeable grid pattern and much sharper picture!



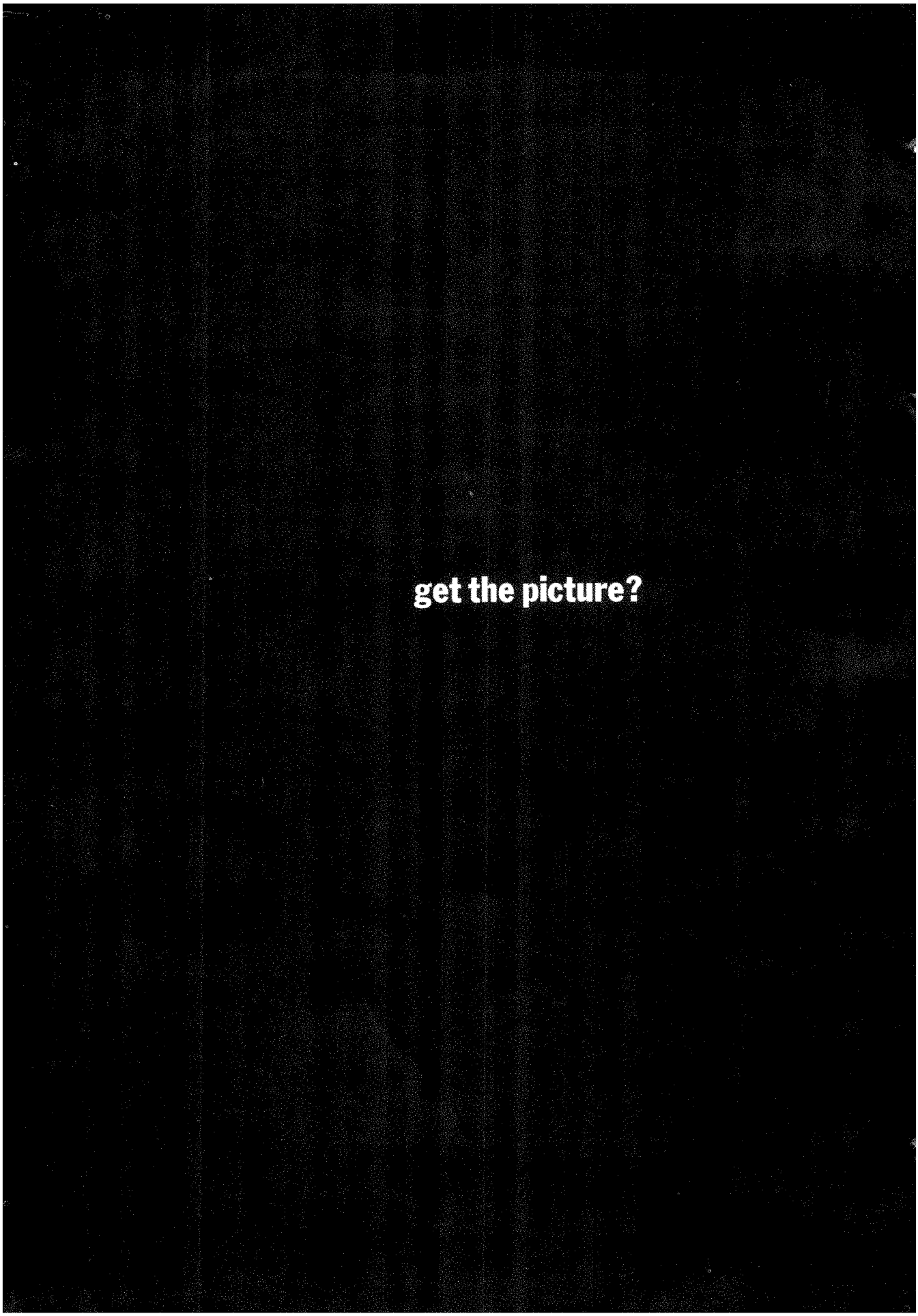
L-F ALUMINUM INTERSPACED GRIDS

the 103 line Ultralūm and the 85 line Micralūm—are made in parallel, focused or crossed types. Available in ratios from 5:1 to 12:1. (May be drilled with electric drill without damage to the internal structure.)

Write for full details or see your x-ray equipment supplier now.

LIEBEL-FLARSHEIM
SYBRON CORPORATION
Cincinnati, Ohio 45215 U. S. A.

Makers of L-F and Franklin X-ray Products


get the picture?

Visualization of the gallbladder, precisely obtained with TELEPAQUE, indicating that there is no cholecystic pathology, permits...
Diagnosis: Normal Gallbladder.

If stones are observed in a gallbladder opacified with TELEPAQUE, function, although impaired, is still present.
Diagnosis: Functioning Gallbladder with stones.

But more importantly, the absence of gallbladder visualization can be of extreme diagnostic significance and ordinarily indicates disease.* Only with TELEPAQUE is it possible to detect those patients with cholecystitis and loss of function since other agents passively opacify the non-concentrating gallbladder.
Diagnosis: Non-functioning Gallbladder.

With TELEPAQUE you get the *complete picture* with outstanding diagnostic dependability and excellent tolerance. Reasons why physicians have long considered TELEPAQUE their oral contrast agent of choice for cholecystography and cholangiography.

*Causes other than disease have been occasionally reported for non-visualizing gallbladders.

Contraindications: Contraindicated in advanced hepatorenal disease or severe impairment of renal function, severe gastrointestinal disorders that prevent absorption, and in patients sensitive to iodine compounds.
Precautions: Severe, advanced liver disease may interfere with metabolism of Telepaque, thus increasing the excretory load on the kidneys. Although renal difficulty has rarely been attributed to Telepaque, renal function should be assessed before cholecystography in severe, advanced liver disease, and renal output and hepatic function should be observed for a few days after the procedure. Patients with preexisting renal disease should not receive high doses of cholecystographic media. Possible renal irritation in susceptible individuals could result in reflex vascular spasm with partial or complete renal shutdown. Caution is advised in patients with coronary disorders, especially those with recent symptoms of coronary artery disease. Blood pressure should be observed after administration of cholecystographic media to these patients. Elevation of protein-bound iodine for several months and false positive urine albumin tests (for three days) may occur after ingestion of iodine-containing cholecystographic media.

Adverse Reactions: Most reactions are mild and transitory; serious side effects are very rare. Gastrointestinal effects (diarrhea, cramps, nausea, vomiting) are the most common. Usually the diarrhea consists merely of a few loose stools, although rarely it may be severe. A mild stinging sensation during urination may occur, and rarely, skin rash, urticaria, pruritus, and flushing. One case of thrombocytopenia has been reported in a patient with a history of conjunctival hemorrhages. Subjective complaints have been: dryness of throat, burning on swallowing, heartburn, sore throat, dizziness, and headache.

Usual Dosage: 3 Gm. (6 tablets) at night after a light supper.

Supplied: Tablets of 500 mg., envelopes of 6 tablets, boxes of 5 and 25 envelopes; also bottles of 500.

Telepaque® for precise oral cholecystography and cholangiography
brand of **iopanoic acid**

TELEPAQUE HAS BEEN USED IN MORE THAN 33,000,000 CASES WITH AN UNPARALLELED RECORD OF CLINICAL SUCCESS

Winthrop PIONEERS IN PRODUCTS FOR RADIOLOGIC DIAGNOSIS

WINTHROP LABORATORIES
NEW YORK, N.Y. 10016

RADIOLOGIST, Board certified or eligible for joint appointment on faculty of Medical College of Georgia and affiliated Dean's Committee, VA Hospital. Special salary arrangements possible. An equal opportunity employer. Contact: Chairman of Radiology Search Committee, LEO G. HORAN, M.D., Veterans Administration Hospital or MARK BROWN, M.D., Chairman, Department of Radiology, Medical College of Georgia, Augusta, Georgia 30904.

HANLEY ECONOMY 14 x 17 X-RAY CABINET
SPECIAL DESIGN SLIDING DOORS
QUALITY AT LOW PRICES
Vertical Filing
We Build Special Size X-Ray Cabinets
SPECIAL SIZE, 33 H x 19½ D x 40 W. W/DOORS
5 COMPARTMENT SIZE—DIVIDERS 14 x 17 .....$121.00
3 COMPARTMENT SIZE—DIVIDERS 14 x 17 ..... 90.00
APPROVAL GUARANTEED—F.O.B. FACTORY—CATALOGUE
HANLEY MEDICAL EQUIPMENT CO.
5814 South Grand X-ray Division St. Louis, Mo. 63111

In reply to advertisers please mention that you saw their advertisement in
THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE
CHARLES C THOMAS • PUBLISHER
Springfield · Illinois

SCHWARZ OBSTETRICAL SLIDE RULE AGAIN AVAILABLE

New improved model 2. Scales and operation identical with original model but new model made of plastic instead of wood.

Slide rule is applicable to a variety of roentgenometry procedures, including the one described by Ball.

Pelvimetry, cephalopelvimetry, estimation of fetal age.

KRAMEX CORPORATION, 18 West 45th Street, New York, N.Y. 10036

(Mail orders accepted)

FOR THE RIGHT ANSWER WHEN YOU NEED IT . . .

- **MEDICAL RADIOGRAPHIC TECHNIC** (3rd Ed., 2nd Ptg.). *Rewritten by* **William L. Bloom, Jr., John L. Hollenbach,** and **James A. Morgan,** *all of the Technical Service X-Ray Dept., General Electric Company, Milwaukee.* '67, 368 pp. (7 × 10), 510 il., 7 tables, $11.00
- **A BIOLOGICAL CONSIDERATION OF TREATMENT OF BREAST CANCER** *by* **George Crile, Jr.,** *Cleveland Clinic, Ohio.* '67, 204 pp., 28 il., 17 tables, $8.00
- **CASE OF THE DAY** *by* **Benjamin Felson** *and* **Jerome F. Wiot,** *both of Univ. of Cincinnati, Ohio.* '67, 96 pp. (6¾ × 9¾), 91 il., $8.50
- **RADIOLOGY AS AN ART AND OTHER ESSAYS** *by* **John L. McClenahan,** *Hosp. of The Univ. of Pennsylvania, Philadelphia.* '67, 104 pp., 3 il., $5.75
- **ILLUSTRATIVE CRANIAL NEURORADIOLOGY** *by* **Alfred L. Schmitz,** *Univ. of California, Los Angeles;* **Samuel B. Haveson,** *Univ. of Southern California, Los Angeles; and* **Duke Hanna,** *Freeman Memorial Hosp., Inglewood.* '67, 404 pp. (8½ × 11), 532 il. (1 in full color), $31.50
- **ERROR AND VARIATION IN DIAGNOSTIC RADIOLOGY** *by* **Marcus J. Smith,** *St. Vincent Hosp., Santa Fe.* '67, 208 pp., 68 il., 18 tables, $8.75
- **TREATMENT FOR CHROMOPHOBE ADENOMA** *by* **Hendrik J. Svien** *and* **Malcolm Y. Colby, Jr.,** *both of Univ. of Minnesota, Rochester.* '67, 116 pp. (6¾ × 9¾), 60 il., 15 tables, $7.50
- **CLINICAL RADIOISOTOPE SCANNING** *by* **Yen Wang,** *Univ. of Pittsburgh, Pa.* '67, 260 pp. (6¾ × 9¾), 280 il., 8 tables, $12.50

CHARLES C THOMAS · PUBLISHER
301-327 East Lawrence Avenue
Springfield · Illinois · 62703

Any minute now, a professional will open that door.





He will be from Ilford

He will be one of our X-ray technical representatives, and within his own specialized field he is as professional as the radiologist himself.

We are particularly proud of our technical representatives. We've tried to make certain that they are carefully trained to be expert in handling the various problems which occur from time to time in every X-ray department. And, we have good reason to believe we have succeeded.

X-ray processing technology is currently undergoing dramatic changes. "Full cycle," "half cycle," and even newer developments have reduced the total processing time of X-ray film from minutes to just seconds.

Chemistry, processors and film have all changed. Ilford technical representatives regard these changes as challenges to their professional know-how and they welcome them. So, next time you have a knotty technical X-ray problem, call in one of our "tech reps". We commend him to you.

He is a professional who can not only assist you with problem-solving but who will be happy to show you how Red Seal on Melinex® will perform in your processing system with Ilfomat chemicals.

ILFORD INC.

West 70 Century Road, P.O. Box 288
Paramus, New Jersey 07652
1217 East El Segundo Boulevard,
El Segundo, California 90245
3566 Elm Street, Hapeville, Georgia 30054

the modern detective story calls for expert police action



You don't uncover stolen jewels sealed in a Maltese falcon. Or deduce just how Colonel Cranshaw was stabbed with the silver stiletto in the hermetically sealed room. Frankly, you're too busy solving the great modern detective story that diagnostic film reading is part of . . . too immersed in the diagnostic process to spend time worrying if the processing chemistry is delivering maximum image quality.

That's where Hunt takes over with the chemistry, service and technical knowledge . . . the expert police action that helps you achieve consistent film development with the ultimate in sensitometric response. Our Sales Representatives are problem solvers. Backed by our service engineer and research laboratory staffs, they're committed to maintaining a totally efficient processing system in your department. To achieve one goal:

More information on any film through total processing control.

HUNT PREMIUM 90/90 DEVELOPER AND REPLENISHER . . . the first ultra-concentrated chemistry for 90 second x-ray processing at the lowest temperature of any product offered to the profession. Premium 90/90 provides the highest contrast and density of any chemistry on the market.

HUNT ULTRA-MAT DEVELOPER AND REPLENISHER . . . the first ultra-concentrated, universal x-ray chemistry for normal temperature ranges accepted for all time cycles . . . 90-seconds, 3½ and 7 minutes. Ultra-Mat has been formulated to meet the speed and contrast levels inherent in the film of your choice with the lowest possible fog level.

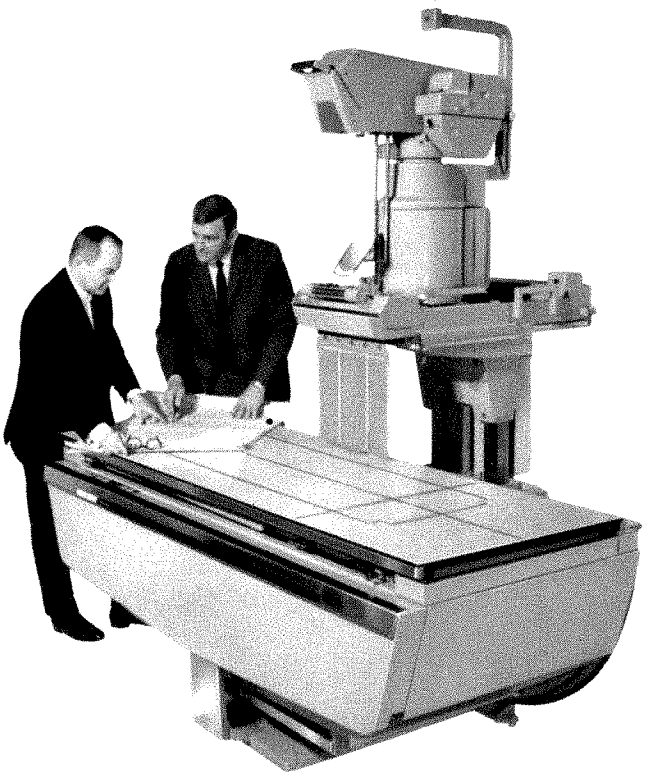
HUNT GRAPH-O-MAT® 90 FIXER-REPLENISHER . . . the recommended and tested fixer for automatic processing systems.

MANUFACTURING CHEMISTS
HUNT
ESTABLISHED 1906

PHILIP A. HUNT CHEMICAL CORPORATION

Palisades Park, New Jersey • Branches in Principal Cities • PHILIP A. HUNT COMPANY (CANADA) LTD. Toronto

MEDICAL SYSTEMS



To buy or not to buy?

That is (no longer) the question.

The question is . . . how? You must keep pace with advances in equipment technology. So, the most obvious—and usually the most desirable—answer is to buy the medical equipment you need. To get immediate possession of the equipment title at maximum savings.

But . . . what if you can't buy. Suppose the funds just aren't there for an outright purchase?

Question no more. Your best answer is Maxiservice®. . . General Electric's full-service leasing and maintenance plan.

No need to ask: does it include all service, preventive maintenance and emergency? Maxiservice does. How about all parts, including x-ray tubes? Of course! Maxiservice wraps up all your equipment needs in one pre-set monthly payment. No surprise bills later. What other lease/maintenance plan includes all this: service and parts . . . plus length-of-your-lease dependability? And, that tells you how much faith General Electric has in the quality of all GE equipment! Simply put, lasting quality means less service and repairs throughout the lease period. Important, too: you can up-date equipment merely by adjusting your agreement.

The decision is yours . . . to buy or not to buy. Whichever is right for you, GE quality and service make your choice easier. Why not talk it over with your GE representative? And, write today for your free, 16-page brochure on Vascular Procedures Room Planning.

Progress is our most important product

GENERAL ELECTRIC

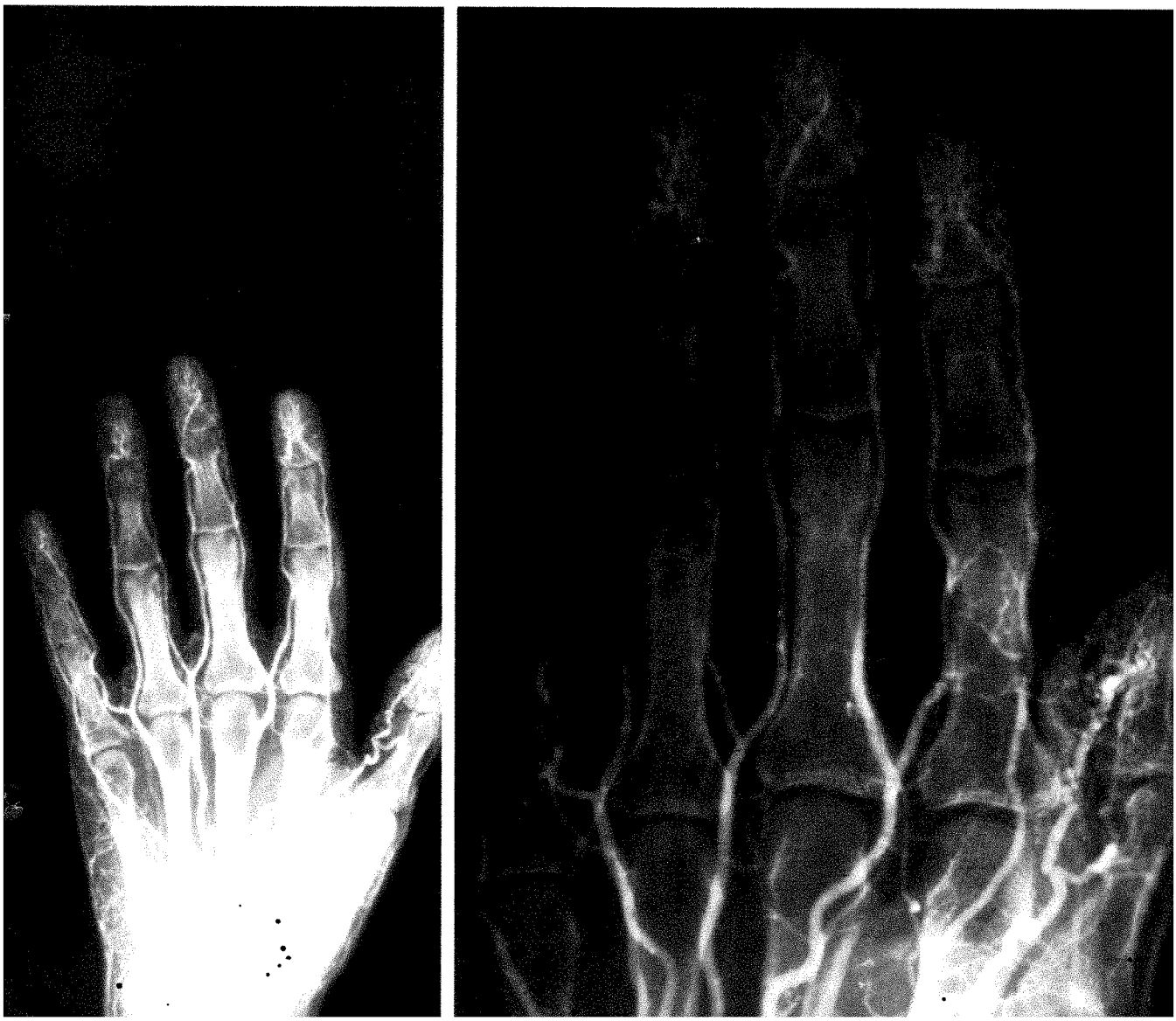
Dept. B2, Milwaukee, Wisconsin 53201

MACHLETT

The Machlett Dynamax "61" X-ray Tube permits the application of direct magnification roentgenography to vascular opacification studies . . . and helps improve diagnostic accuracy.

Conventional arteriogram

Direct serial magnification arteriogram



MACHLETT

The arteriograms on the preceding page demonstrate the increased information available with direct serial magnification compared to routine angiography.

The x-ray tube recommended for making these examinations is the Machlett Dynamax "61", a specialized version of the Dynamax "60". This fine-focus x-ray tube is capable of operating at the higher loadings required for rapid sequential short exposures.

The Dynamax "61" is also designed for high-energy angiography as well as enlargement radiography. In addition, it extends cine-radiographic and spot film capabilities.

Ratings and Characteristics

Maximum Peak Voltage	150 PKV (Anode to cathode)
Anode Heat-Storage Capacity	200,000 HU
Insert Tube Target Angle	10°
Insert Tube Anode	Rotary type with rhenium tungsten faced molybdenum target of high heat-storage and cooling capacity.
Focal Spot Combinations Available	0.3mm small focal spot with 1.0mm large focal spot

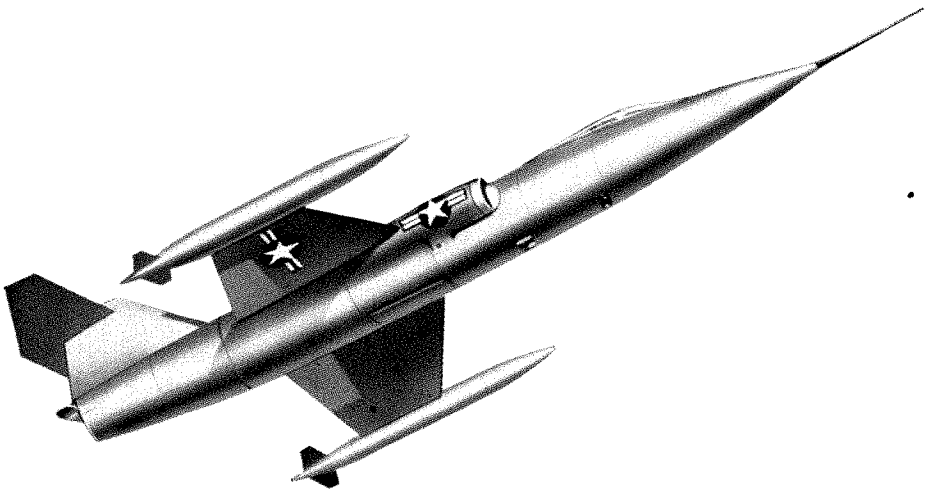
Write for a copy of "An Atlas of Serial Magnification Roentgenography," a 32-page booklet containing comparisons of cerebral, vertebral, pulmonary, renal, celiac, mesenteric, hand and wrist arteriograms obtained by direct serial magnification and by conventional techniques. Complete technical information is also available covering the Dynamax "61" tube. The Machlett Laboratories, Inc., 1063 Hope Street, Stamford, Conn. 06907.



RAYTHEON

THE MACHLETT LABORATORIES, INC.

A SUBSIDIARY OF RAYTHEON COMPANY



Fastest X-Ray screens made. Rādelin® STF-2

Radelin STF-2's are the fastest X-ray screens made, and they've been the fastest for years.

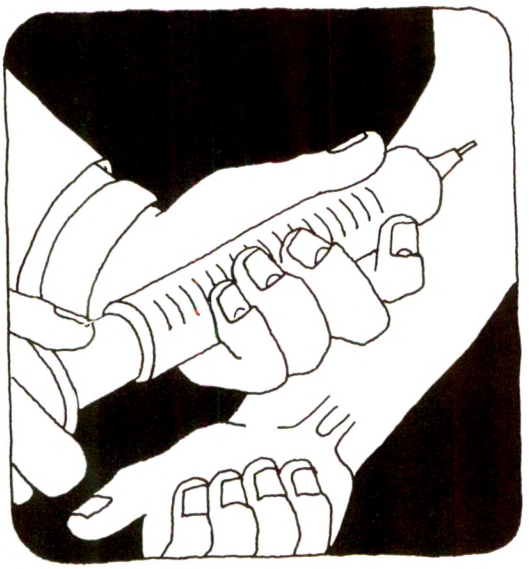
STF-2's are at least 30% faster than your present high speed screens. Their resolution provides excellent definition even at STF-2's extremely high speed; makes them ideal for high Kv, portable, spot film and roll film technics as well as for routine radiography — minimizing patient exposure.

Get speed, clarity and durability. Go with the best; Radelin STF-2. The fastest X-ray screen you can buy.

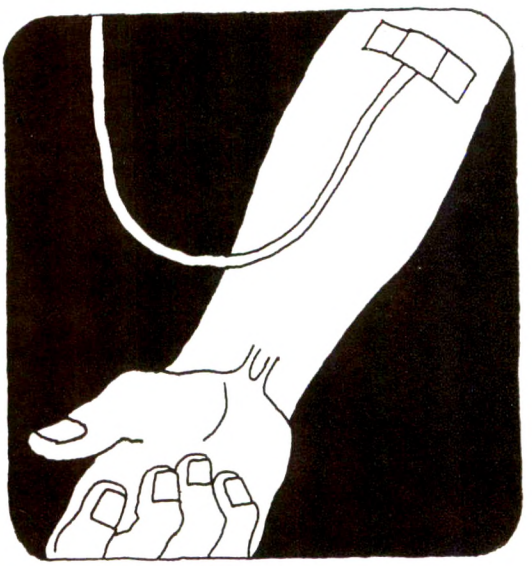
USR

RĀDELIN MEDICAL PRODUCTS
UNITED STATES RADIUM CORPORATION
MORRISTOWN, NEW JERSEY 07960

Now...2 important I.V. Radiodiagnostic procedures for improved visualization



Adequate Dose Urography
with 50-60 ml. of 50% solution



Drip Infusion Pyelography
using between 250-400 ml. of a 25% solution*

Hypaque® 50%
sodium

brand of **sodium diatrizoate**

Winthrop

PIONEERS IN PRODUCTS FOR RADIOLOGIC DIAGNOSIS

*By diluting the 50% solution with an equal amount of sterile water for injection, USP, sodium chloride injection, USP, or dextrose injection, 5%, USP.

(Please see summary on following pages)

Hypaque® 50%
sodium
brand of **sodium diatrizoate**

Excretory Urography and Drip Infusion Pyelography

Description: Hypaque sodium is a sterile aqueous solution of sodium 3,5-diacetamido-2,4,6-triiodobenzoate, a radiopaque medium used to delineate internal structures.

Warning: Do not use Hypaque sodium for myelography. Injection of even a small amount into the subarachnoid space may produce convulsions and result in fatality.

General and Specific Precautions: Caution is advised in patients with a history of bronchial asthma, other allergic manifestations, or of sensitivity to iodine; these conditions represent a special risk, though not an absolute contraindication. To avoid or minimize possible allergic reactions, premedication with antihistamines may be considered. Benadryl (diphenhydramine hydrochloride) in the same syringe with Hypaque may result in precipitation. A test dose of contrast medium is not entirely reliable. Severe reactions, including fatalities, have occurred with a test dose as well as with the full diagnostic dose.

Caution is advised in patients with severe cardiovascular disease. In patients with impaired renal function and cardiovascular disease, drip infusion pyelography imposes a sudden osmotic and sodium load which can precipitate congestive heart failure. Contrast media injected into arteries or veins can promote sickling of red cells in susceptible individuals. In patients with reduced renal function, repeat of excretory or retrograde pyelography should be delayed at least 48 hours to avoid temporary suppression of urine. In preparation for excretory urography of patients with multiple myeloma, partial dehydration is not recommended, since this may predispose to the precipitation of myeloma protein in the kidney tubules. When thyroid function studies (PBI and 24-hour radioiodine uptake levels) are indicated, they should be performed *prior* to radiographic studies or several days afterwards, to avoid inaccurate results.

Hypaque sodium 50% should always be injected at body temperature.

General and Specific Adverse Reactions: Adverse reactions, usually of a minor nature, have occurred in 10-14 per cent of patients who have received Hypaque intravenously. Reactions due to *faulty technique* include hematomas and ecchymoses, following extravasation from the vein, and pyrogenic reactions. *Hemodynamic reactions* include vasodilatation with flushing, hypotension and, rarely, vein cramp or thrombophlebitis. Serious *cardiovascular reactions* include rare cases of cardiac arrhythmias (e.g., ventricular fibrillation), shock, and cardiac arrest. Transient proteinuria may occur occasionally following the injection of radiopaques and, rarely, oliguria and anuria have been reported secondary to a hypotensive reaction. *Allergic reactions* include asthmatic attacks, nasal and conjunctival symptoms, cutaneous reactions such as urticaria and, rarely, anaphylactic shock, sometimes with fatal outcome. Severe reactions may also be manifested by signs and symptoms relating to the *respiratory system* (dyspnea, cyanosis, pulmonary or laryngeal edema), or to the *nervous system* (restlessness, confusion, or convulsions). *Other reactions* include nausea, vomiting, excessive salivation, anxiety, headache, and dizziness. Infrequently, "iodism" (salivary gland swelling) from organic compounds appears two days after exposure and subsides by the sixth day. Reactions to drip infusion pyelography may not appear until some hours after the examination.

Angiography (Peripheral Arteriography and Venography)

Precautions *(See also General Precautions):* Extreme caution is advised in considering peripheral arteriography in patients suspected of having thromboangiitis obliterans (Buerger's disease). Any procedure (even needling or insertion of a catheter) may induce a severe arterial and/or venous spasm. Caution is also advisable in patients with severe ischemia associated with ascending infection.

Adverse Reactions *(See also General Adverse Reactions):* In addition to those listed under General Adverse Reactions, are those due to arterial trauma during the procedure (i.e., needling, insertion of catheter, subintimal injection, perforation, etc.) as well as to the hypertonicity or effect of the medium; also reported are transient arterial spasm, extravasation, hemorrhage, hematoma with tamponade, injury to nerves proximal to artery, thrombosis (rare in venography; if vein is irrigated following injection), dissecting aneurysm, arteriovenous fistula, (e.g., with accidental perforation of femoral artery and vein during needling) transient leg pain from contraction of calf muscles in femoral arteriography; transient hypotension after intraarterial (brachial) injection, and brachial plexus injury with axillary artery injections.

Cerebral Angiography: Because of the special techniques required, it is recommended that Hypaque sodium be used for this purpose only by persons skilled and experienced in carrying out this procedure.

Contraindication: Carotid angiography should be avoided during the progressive period of a stroke, since this increases the risk of cerebral complications.

Precautions *(See also General Precautions):* Select patients for this procedure with care. Use the 50 per cent solution with caution in extreme senility (but not old age, *per se*); advanced arteriosclerosis; severe hypertension; and cardiac decompensation.

The diagnostic value of the procedure, according to many authorities, when employed early enough in locating lesions amenable to surgery, may outweigh the added risk to patients who have recently experienced cerebral embolism or thrombosis (stroke syndrome). A small number of postangiographic fatalities, including progressive thrombosis, have occurred in which the procedure did not appear to play a role. Patients with severe cerebrovascular disease may be examined primarily by indirect methods of angiography.

Care should be exercised to avoid contaminating catheters, syringes, needles, and contrast media with glove powder or cotton fibers.

Angiography is hazardous in subarachnoid hemorrhage. In migraine, the procedure can be hazardous because of ischemic complications, particularly if performed during or soon after an attack.

Adverse Reactions *(See also General Adverse Reactions):* The major sources of complications are faulty technique, occlusive atherosclerotic vascular disease, repeated injections of the contrast media, and higher doses than those recommended.

Untoward reactions are mostly mild and transient, although permanent visual field defects and deaths have been reported.

(continued on next page)

(continued from preceding page)

Hypaque® 50%
sodium
brand of **sodium diatrizoate**

Vascular reactions: flushing, vessel spasm, thrombophlebitis, and cutaneous petechiae.

Neurologic complications: transient cerebral blindness, neuromuscular disorders, convulsions, coma, hemiparesis, unilateral dysesthesias, visual field defects, aphasia, and respiratory difficulties.

Aortography

Precautions *(See also General Precautions):* Special caution is advised to avoid inadvertent intrathecal injection when using the translumbar technique. The incidence and severity of reactions or complications that may occur are influenced by: the care and experience with which the procedure is performed; the amount and type of medium used; the age and condition of the patient; and the premedication and anesthesia used. Since aortography is not without some danger, it should be performed only by those experienced in the technique. Wherever possible, repeated injections of the solution during a single study should be avoided.

Adverse Reactions *(See also General Adverse Reactions):* Renal damage and shutdown; neurologic complications such as transverse myelitis or paraplegia; cardiovascular complications such as shock, cardiac arrest or failure, coronary occlusion, arterial thrombosis, embolism, and perforation of vessels; extravasation or hemorrhage from the puncture site or retroperitoneal catheter perforation; necrosis of the intestinal wall; acute pancreatitis; deaths; diffuse cutaneous petechiae; subintimal injection and aortic dissection.

Intraosseous Venography

See General Precautions and Adverse Reactions. A general anesthetic is sometimes necessary since the method is painful. Occasionally, extravasation of the contrast medium from the needle into the soft tissue may occur.

Direct Cholangiography

Precaution *(See also General Precautions):* This procedure should be used with caution in the presence of acute pancreatitis, injecting no more than 5 to 10 ml. without undue pressure.

Adverse Reactions *(See also General Adverse Reactions):* These may be attributed to injection pressure or excessive volume of the medium, resulting in overdistention. Such pressure may produce a sensation of epigastric fullness, followed by moderate pain in the back or right upper abdominal quadrant, which will subside when injection is stopped.

Some of the medium may enter the pancreatic duct and cause a transient serum amylase elevation 6 to 18 hours later, without apparent ill effects. Pancholangitis resulting in liver abscess has been reported. Occasionally, nausea, vomiting, fever, and tachycardia have been observed.

Hysterosalpingography

Contraindications: Menstruation, active or imminent; infection in any part of the genital tract, including the external genitalia; pregnancy, known or suspected. Use not advised for six months after end of pregnancy, or 30 days after conization or curettement.

Precaution *(See also General Precautions):* Caution should be exercised in patients with known or suspected carcinoma to avoid possible spread of the lesion by the procedure.

Splenoportography

Precautions *(See also General Precautions):* Procedure should be performed with caution on patients with blood dyscrasias, a tendency to severe bleeding, or a spleen recently become tender and palpable.

Adverse Reactions *(See also General Adverse Reactions):* Persistent hemorrhage with hemoperitoneum has been reported, and, in some instances, hemorrhage has required splenectomy.

How Supplied: Ampuls of 30 ml., boxes of 1, 10, and 25. A 1 ml. sensitivity test ampul is furnished with each ampul. Vials of 20 and 30 ml., rubber stoppered, boxes of 1, 10, and 25. Vials of 50 ml., rubber stoppered, boxes of 1 and 10. Each vial contains sufficient excess to permit withdrawal of 1 ml. for testing sensitivity.

If the solution is chilled, crystals may form but will readily dissolve if the ampul or vial is placed in moderately hot water before use. Cool to body temperature before injecting.

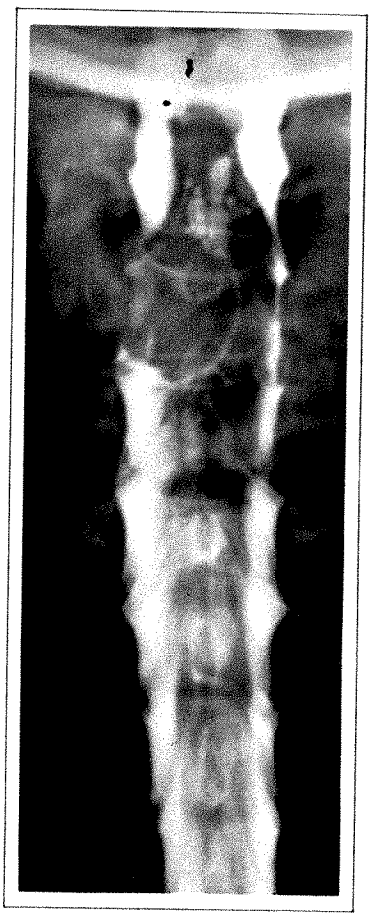
Winthrop

WINTHROP LABORATORIES, New York, New York 10016

PIONEERS IN PRODUCTS FOR RADIOLOGIC DIAGNOSIS

The cervical myelogram illustrated here is an interesting demonstration of a relatively large neurofibroma in the spinal canal at the level of the third cervical vertebra.

During the first manipulation of Pantopaque® contrast medium into the cervical subarachnoid space, image of the column of contrast material was interrupted at the C-3 level, particularly on the right, and gave a first impression of the presence of a nonencapsulated, infiltrating, intramedullary tumor, which appeared to enlarge the spinal cord. On further manipulation, caudally, however, a thin stream of contrast material diverged to the left and outlined medial, upper, and lower borders of a well-circumscribed tumor.



The patient, a 58-year-old woman, had had cramping of the foot muscles, especially on the right, for about three years. Eight months prior to examination, she began to experience dull pain in the back of the head and stiffness of the lower limbs when descending stairs. About two months prior to myelography, she began to notice "pins and needles" sensations in all limbs, again particularly on the right, and developed difficulty in using her right upper limb.

The tumor was excised following laminectomy of the third, fourth, and fifth vertebrae and the spinal cord was thoroughly decompressed. The patient did very well postoperatively and today is an essentially well woman.

Side Effects. Clinical reports indicate that the incidence and the severity of the side effects following Pantopaque myelography with aspiration of the medium is but slightly greater than with ordinary lumbar puncture. In 10-30 percent of such cases there may be transient symptomatic reactions consisting of slight temperature elevation and increase of symptoms referable to a back condition. When the medium is not removed, similar transient side effects occur with a slight elevation of temperature in a greater percent of patients. To reduce the reactions to a minimum and to facilitate the absorption of the medium, the bulk of the Pantopaque should be removed by aspiration after myelography.

Contraindications. Pantopaque should not be injected where a lumbar puncture is contraindicated, nor within 10 days of a previous lumbar puncture. The latter precaution is necessary to avoid subdural and extra-arachnoid extravasation. An injection should not be carried out until the operator is certain that his needle is in the subarachnoid space.

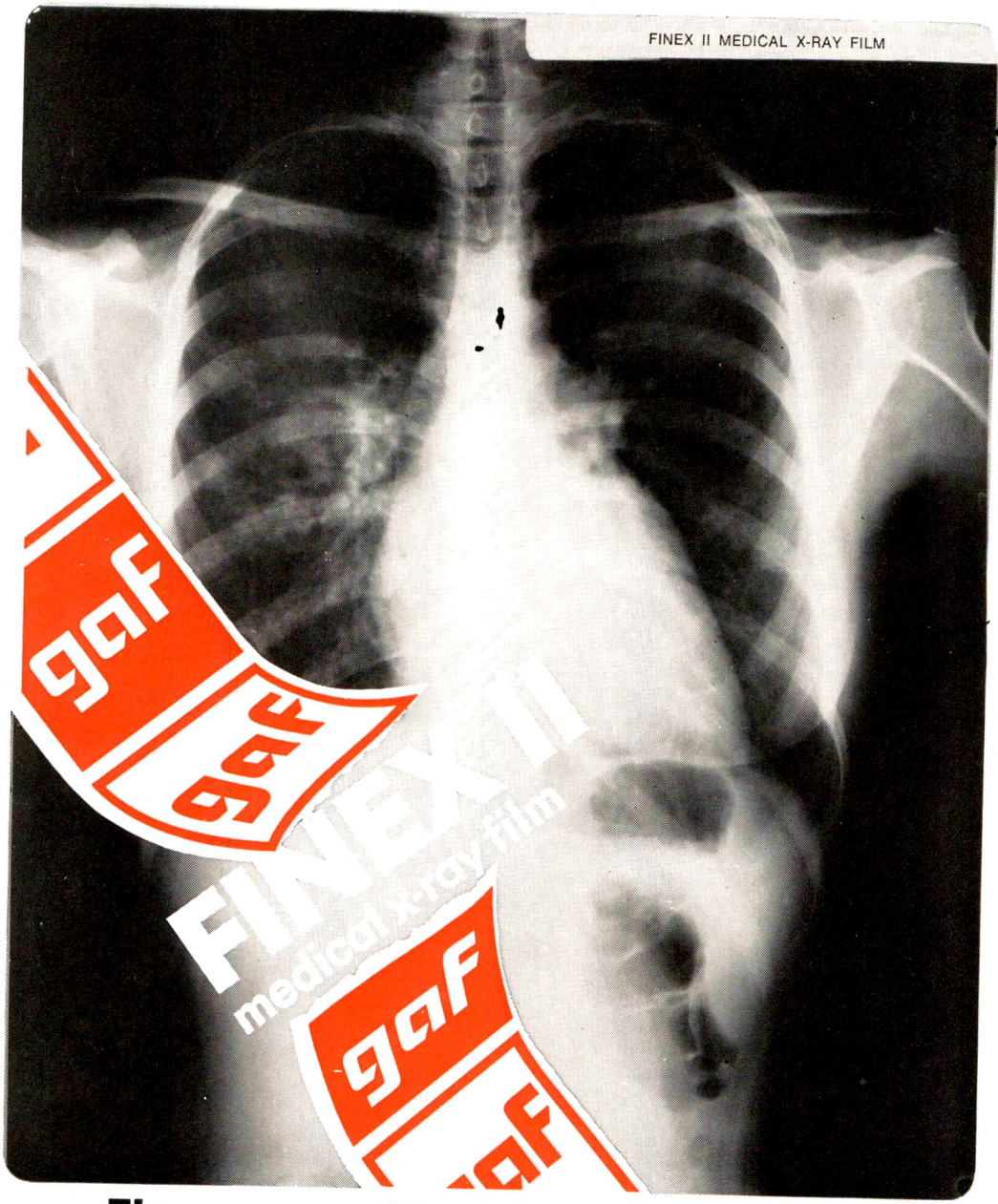
Limitations. Pantopaque has not been studied adequately from a clinical standpoint as a contrast medium for body cavities other than the subarachnoid space. The limitations and contraindications in other areas are not known.

Pantopaque, the trademark under which all leading x-ray dealers supply the compound ethyl iodophenylundecylate, is prepared as the myelographic contrast medium Iophendylate Injection, U.S.P. by Lafayette Pharmacal Inc., Lafayette, Indiana 47904. Pantopaque is a registered trademark of Eastman Kodak Company.

INDEX TO ADVERTISERS

Abbott Laboratories ..... xxvi, xxvii
AGA Corporation viii
Amersham/Searle Corporation ..... lxxvi, lxxvii
Ames Color-File Corporation lxvii
Atomic Energy of Canada Ltd. vii
Automatic Seriograph Corporation, The (Div. of Litton Industries) xxi
Baird-Atomic, Inc. ..... xxx, xxxi
Barnes-Hind Barium Products lxxviii
Baruch Instruments Corporation ..... lxxxvi, lxxxvii, lxxxviii
Becton-Dickinson (Div. of Becton, Dickinson and Company) xxviii
Bell-Craig, Inc. lxxiii
Brayten Pharmaceutical Co. vi
Cenco X-Ray Company ..... xl, xli
Dunlee Corporation ..... liii, liv, lv
Eastman Kodak Company lxxii
Elema-Schonander, Inc. lxxiv
E-Z-Em Company lvi
Fleet Co., C. B., Inc. ..... lxv, lxvi, cv
GAF Corporation ..... ix, x, xi, xii, xcvi
General Electric Company xxiv
Green, Warren H., Inc. xx
Halsey X-Ray Products Company xcii
Hanley Medical Equipment Company i
High Voltage Engineering ..... xciv, xcv
Hunt, Philip A., Chemical Corporation xciii
Ilford, Inc. lxxxii
Isotopes xcii
Kramex Corporation ciii
Lafayette Pharmacal, Inc. lxxxix
Liebel-Flarsheim Company (Div. of Ritter-Pfaudler Corporation) ..... xcvii, xcviii
Machlett Laboratories, Inc. ..... lxx, lxxi
Mallinckrodt/Nuclear Radiopharmaceuticals lxxviii
McElroy, Donald, Inc. xxv
3M Company (X-Ray Division) ..... lviii, lix, lx, lxi, lxii, lxiii
Neisler Laboratories lxiv
Nicholas Laboratories, Ltd. ..... xxxviii, xxxix
Nuclear-Chicago Corporation lxxv
Ohio-Nuclear, Inc. ..... Second Cover
Picker Nuclear Corporation ..... xxxii, lvii, Fourth Cover
Picker X-Ray Corporation ..... xxii, xxiii
Profexray, Inc. v
Purdue Frederick Company, The xiii
Pyne X-Ray Corporation xlii
Schick X-Ray Company ..... xxxiii, xxxiv
Siemens Medical of America, Inc. .....
Squibb, E. R., & Sons, Inc. ..... xv, xvi, xvii, xxix, xxxv, xxxvi, xxxvii, lxviii, lxix, lxxix, lxxx, lxxxi
Thomas, Charles C, Publisher ..... xcii, cvi
United States Radium Corporation xcix
U. S. Veterans Administration Hospital (Augusta, Ga.) xcii
Varian Radiation Division ..... xviii, xix
Westinghouse X-Ray Division ..... lxxxiii, lxxxiv, lxxxv
Winthrop Laboratories ..... xliii, xliv, xlv, xlvi, xlvii, xlviii, xlix, l, li, lii, xc, xci, c, ci, cii
Wolf X-Ray Corporation ..... Third Cover

We try to present an accurate index. Occasionally this may not be possible because of a last-minute change or an omission.



Fine —

Finex™ II is an extra-fine grain film on a polyester base. Can be used in all processing systems, automatic and manual.

Finer —

Finex II gives a finer radiographic image, and dries better in marginal processing. No base fog.

FINEX II

A medium speed, 90 second film. Completely interchangeable. The perfect complement to GAF-X® film.

* Trademark of GAF Corporation

gaf

GAF Corporation
140 West 51 Street, New York, N.Y. 10020

WHEN YOUR SPECIALTY IS ROENTGENOLOGY

17 Books Selected from the Thomas Catalog of over 2100 Titles . . .

☐ **THE CARE OF RADIATION CASUALTIES** *by* **John Blakely,** *Medical Officer-in-Charge, United Kingdom Atomic Energy Authority.* '68, 136 pp., 17 il. (1 in color), 10 tables, $5.50

☐ **SELECTIVE RENAL ARTERIOGRAPHY: Its Application to the Diagnosis of Renal Vascular and Parenchymal Lesions** *by* **Ivan L. Bunnell,** *State Univ. of New York at Buffalo.* '68, 248 pp. (6¾ × 9¾), 183 il., $18.75

☐ **AN ATLAS OF PATHOLOGIC PNEUMOENCEPHALOGRAPHIC ANATOMY** *by* **Giovanni Di Chiro,** *National Institute of Neurological Diseases and Blindness, Bethesda, Md.;* **Mannie M. Schechter,** *Albert Einstein College of Medicine, New York City; and* **Ingmar Wickbom,** *Univ. of Gothenburg Medical School, Sweden.* '67, 594 pp. (11 × 8½), 926 il. (5 in color), $49.50

☐ **X-RAY DIAGNOSIS OF CONGENITAL CARDIAC DISEASE** *by* **Larry P. Elliott** *and* **Gerold L. Schiebler,** *both of Univ. of Florida College of Medicine, Gainesville. Foreword by* **Paul C. Hodges.** '68, 260 pp., 221 il., 3 tables, $11.50

☐ **PRINCIPLES OF RADIOGRAPHIC EXPOSURE AND PROCESSING (2nd Ed., 5th Ptg.)** *by* **Arthur Fuchs,** *Rochester, N.Y.* '68, 304 pp. (7 × 10), 600 il., $11.00

☐ **FUNDAMENTAL PROBLEMS IN SCANNING** *compiled and edited by* **Alexander Gottschalk** *and* **Robert N. Beck,** *both of Univ. of* Chicago. *(38 Contributors)* '68, 424 pp. (7 × 10), 309 il. (10 in full color), 12 tables, $26.75

☐ **ROENTGENOGRAPHIC DIAGNOSIS OF BLADDER TUMORS** *by* **Erich K. Lang,** *Methodist Hosp., Indianapolis.* '68, 132 pp. (7 × 10), 94 il., 11 tables, $9.75

☐ **HODGKIN'S DISEASE** *compiled and edited by* **David W. Molander,** *Cornell Univ. Medical College, and* **George T. Pack,** *New York Medical College. Both of New York City. (7 Contributors)* '68, 228 pp. (7 × 10), 121 il., 39 tables, $15.00

☐ **AIDS TO ETHICS AND PROFESSIONAL CONDUCT FOR STUDENT RADIOLOGIC TECHNOLOGISTS (2nd Ed.)** *by* **James Ohnysty,** *St. Francis Hosp., Colorado Springs.* '68, 172 pp., $6.75

☐ **ROENTGENOLOGY OF THE SPLEEN AND PANCREAS** *by* **Josef Rosch,** *Charles Univ., Prague, Czechoslovakia.* '67, 376 pp. (6¾ × 9¾), 434 il., $29.75

☐ **SOLITARY METASTASES** *by* **Philip Rubin,** *Univ. of Rochester Medical Center, New York, and* **Jerold Green,** *Zellerbach Saroni Tumor Institute, Mt. Zion Hosp., San Francisco.* '68, 268 pp., 153 il., 30 tables, $14.75

☐ **CANCER THERAPY BY INTEGRATED RADIATION AND OPERATION** *compiled and edited by* **Benjamin F. Rush, Jr.,** *and* **Robert H. Greenlaw,** *both of Univ. of Kentucky College of Medicine, Lexington. Foreword by* **Charles Tucker.** *(40 Contributors)* '68, 176 pp. (7 × 10), 58 il., 82 tables, $12.75

☐ **LUNG CALCIFICATIONS IN X-RAY DIAGNOSIS** *by* **Emanuel Salzman,** *Univ. of Colorado School of Medicine, Denver.* '68, 132 pp. (6¾ × 9¾), 74 il., $7.50

☐ **THE FUNDAMENTALS OF X-RAY AND RADIUM PHYSICS (4th Ed., 5th Ptg.)** *by* **Joseph Selman,** *Univ. of Texas, Tyler.* '69, 498 pp., 306 il., 16 tables, $10.50

☐ **CERVICAL SPONDYLOSIS AND ITS NEUROLOGICAL COMPLICATIONS** *by* **Bernard H. Smith,** *State Univ. of New York at Buffalo.* '68, 240 pp. (6¾ × 9¾), 101 il., $12.00

☐ **NORMAL RADIOLOGICAL ANATOMY: Radiological Optics and Film Interpretation** *by* **Henry Tillier,** *Late Professor of Radiology, Algiers. Translated and edited by* **Ronan O'Rahilly,** *St. Louis Univ. School of Medicine.* '68, 400 pp., 375 figs., 3 tables, $12.50

☐ **ADVANCES IN DYNAMIC RADIOACTIVE SCANNING** *compiled and edited by* **Yen Wang,** *Univ. of Pittsburgh, Pa. (10 Contributors)* '68, 140 pp., 101 il., 7 tables, $8.50

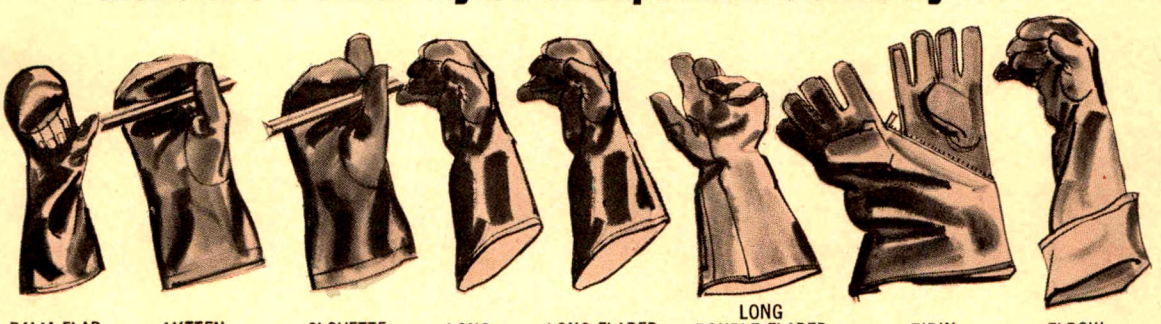
CHARLES C THOMAS • PUBLISHER 301-327 East Lawrence Ave. **SPRINGFIELD • ILLINOIS • 62703**

THIS IS A WOLF SUPERFLEX GLOVE



It would be called the world's finest X-ray glove except for one thing...

there are 8 other styles of Superflex Gloves by WOLF



PALM FLAP | MITTEN | GLOVETTE | LONG | LONG FLARED | LONG DOUBLE FLARED | ZIPIN | ELBOW

Next time you're ready to purchase x-ray gloves, remember the name WOLF SUPERFLEX... its your assurance of the highest degree of protection, flexibility, comfort and durability available. Each of the above styles are made in three protective values (.25mm, .5mm, .75mm)... as well as custom made to meet special length and/or added protective requirements.

WOLF SUPERFLEX GLOVES—TOUGHEST LITTLE SOFTIES IN THE BUSINESS

WOLF X-RAY CORPORATION · Wolf · NEW YORK

WOLF X-RAY CORPORATION

NEW YORK • CHICAGO • LOS ANGELES • TORONTO

Executive Offices: 182-20 LIBERTY AVENUE, JAMAICA, NEW YORK 11412

AFFILIATES: WOLF DENTAL FILM MOUNT CORP. • WOLF RADIATION PROTECTION CORP.

Somewhere near you, a radiologist is getting the sharpest images he's ever seen because of this new table.

Hundreds of radiologists now working with the new Picker "Galaxy" table are getting the best images they've ever experienced: the sharpest fluoroscopy, spotfilms, and Bucky radiographs. And because their everyday practical experience is likely to be more revealing than our technical explanations, you might wish to seek out a current user of the "Galaxy" table. (If you need help with this search, let us know. We'll help you set up a visit.)

Until then, the following technical explanations can provide background as to why the "Galaxy" table produces such superb images.

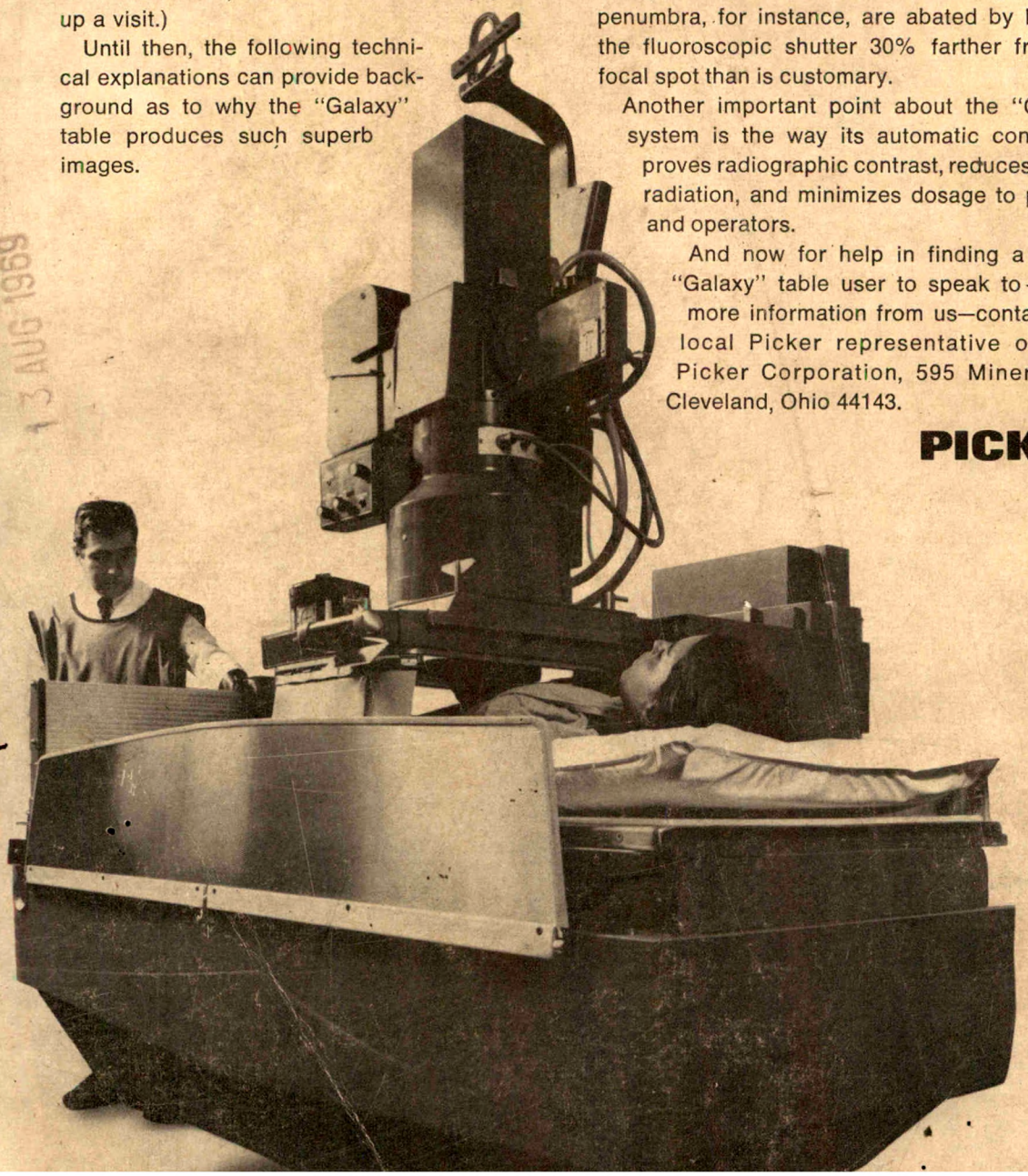
The table is so structurally rigid that it thoroughly tames the subtle (and some not-so-subtle) vibrations all too often encountered in x-ray tables. The improvement in image sharpness resulting from such suppression is dramatic.

The "Galaxy" collimating system optimizes imaging geometry by significantly refining the relationship of focal spot, shutter plane, film plane, and patient plane. Geometric unsharpness and penumbra, for instance, are abated by locating the fluoroscopic shutter 30% farther from the focal spot than is customary.

Another important point about the "Galaxy" system is the way its automatic coning improves radiographic contrast, reduces scatter radiation, and minimizes dosage to patients and operators.

And now for help in finding a nearby "Galaxy" table user to speak to—or for more information from us—contact your local Picker representative or write Picker Corporation, 595 Miner Road, Cleveland, Ohio 44143.

PICKER



13 AUG 1959